A THESIS REPORT ON

FUNCTIONAL ASSESSMENT AND ELECTROMYOGRAPHIC PATTERNS IN FOCAL HAND DYSTONIA

Submitted in partial fulfillment of the requirements
for the degree of D.M. Neurology Branch I
of
Tamil Nadu Dr. MGR Medical University

DEPARTMENT OF NEUROLOGICAL SCIENCES
CHRISTIAN MEDICAL COLLEGE, VELLORE

FUNCTIONAL ASSESSMENT

AND

ELECTROMYOGRAPHIC PATTERNS

IN

FOCAL HAND DYSTONIA

CERTIFICATE

This is to certify that the Dissertation titled “Functional Assessment and Electromyographic patterns in Focal Hand Dystonia” is the bonafide work of Dr. Ajith Sivadasan submitted in fulfillment of the DM – Neurology examination conducted by the Tamil Nadu Dr. M.G.R Medical University, Chennai, in August 2010.

Dr. Suresh Devasahayam,
Professor and Head,
Department of Bioengineering,
Christian Medical College
Vellore.

CERTIFICATE

This is to certify that the Dissertation titled “Functional Assessment and Electromyographic patterns in Focal Hand Dystonia” is the bonafide work of Dr. Ajith Sivadasan submitted in fulfillment of the DM – Neurology examination conducted by the Tamil Nadu Dr. M.G.R Medical University, Chennai, in August 2010.

Prof. Ari George Chacko M.ch (Neuro)
Professor of Neurosurgery and Head,
Department of Neurological Sciences,
Christian Medical College
Vellore.

ACKNOWLEDGEMENT

It is my pleasure to acknowledge the guidance, help and support provided to me by many while doing this work.

I sincerely thank my respected teacher and guide **Dr. Mathew Alexander**, Professor & Head, Neurology for his guidance, ideas, motivation and timely suggestions without which this dissertation would not have been possible.

I would also like to acknowledge the contribution of Dr**. Suresh Devasahayam**, Professor & Head, Dept. of Bioengineering for his invaluable help in devising the software and 16 channel electrodes for EMG data acquisition, guidance, support and timely suggestions.

I also thank **Dr. K. Srinivasa Babu**, Senior Scientist, Division of Neurophysiology, Dept. of Neurological Sciences for his suggestions, support and provision of all required facilities.

I am highly indebted to **Mr. M. Sanjay**, Senior Registrar, Dept. of Bioengineering for his help and support in setting up the software and electodes for EMG data acquisition, his involvement in data collection, analysis and providing timely suggestions.

I thank all the subjects who have taken part in the study for spending their valuable time and their cooperation during data recording.

I also sincerely acknowledge the support provided by the entire faculty, Dept of Neurology – **Dr Sanjith Aaron, Dr Vivek Mathew, Dr Maya Thomas, Dr Manoj Goyal, Dr Anil K Patil and Dr Amit Srivastava** during completion of this dissertation.

I thank my colleagues **Dr Krishnan, Dr Ajith, Dr Zeyaur Rahman Azad, Dr Karthik and Dr Shubrankshu** for their co-operation.

I also acknowledge the contribution of **Mrs Vijayalakshmi (Neurocomputers), Mrs Vasantha (secretary) and Mrs Nirmala, Mr Adi, Mr Senthil, Mr Paul (EMG lab)** at various stages of the study.

I thank my **family** for their love, prayers and moral support during the entire period while doing the study.

Above all, I thank **Almighty** for all his blessings without which the study would not have been possible.

LIST OF ABBREVIATIONS

ADP: Adductor Pollicis

APB: Abductor Pollicis Brevis

BNT: Botulinum Toxin

BIC: Biceps

EDC: Extensor Digitorum Communis

EMG: Electromyogram

FDS: Flexor Digitorum Superficialis

FES: Functional Electrical Stimulation

FHD: Focal Hand Dystonia

LICI: Long Intracortical Inhibition

MEP: Motor Evoked Potential

SCM: Sternocleidomastoid

SEMG: Surface Electromyography

SICI: Short Intracortical Inhibition

SMO: Sensori-Motor Organisation

TMS: Transcranial Magnetic Stimulation

TRIC: Triceps

TRPZ: Trapezius

WC: Writer's Cramp

ABSTRACT

INTRODUCTION: Treatment options for FHD still remain limited and suboptimal. Surface EMG provides a rational approach to clinical assessment and could guide selection and monitoring of appropriate therapy in subjects with Focal Hand Dystonia. However, data on the EMG patterns are relatively scarce. The correlation of the various electrophysiological phenomenon can have important treatment implications and evolve novel therapies.

OBJECTIVES: To study the ontogeny, recruitment pattern, motor activity and spread of flow of muscle contractions during different phases of a "writing task" using surface EMG recordings in the distal, intermediate and proximal group of muscles in both the upper limbs and correlate the EMG parameters with functional disability.

METHODS: Surface EMG was obtained from 4 pairs of muscles in both the upper limbs using 16 channels. Recording and analysis of the data was done using customized software. FHD group was compared with normative controls with regard to EMG patterns obtained during the phases (rest, anticipation of writing, writing, relaxation) of the "writing task". Burke Fahn Marden scale was used as an index for severity of dystonia. Rectified mean SEMG was calculated. Ontogeny, recruitment, flow of activity and mirror movements were analyzed. Legibility and speed of writing were indicators for functional disability. Student 't' test and Chi-square test were used for group comparisons. Mann-Whitney test was used for non-parametric variables.

RESULTS: Total of 36 subjects (20 FHD and 16 controls) were included. 50% of the FHD group was treatment naïve, 70% had FMS 3 dystonia and 45% had illegible handwriting. Mean time taken for writing was significantly longer in FHD (8'6" versus 3'25"). "Early onset" during anticipatory phase was seen in 60%, mean time being 32.4 seconds. The EMG amplitudes were significantly higher during writing, "delayed offset" was also seen in 90%, mean time 33 seconds. Rapid recruitment was noted, there was faster spread of activity to EDC, TRPZ and BIC. Mirror movements were identified in 100%, higher EMG amplitudes were also noted in the normal limb compared to controls. Spectral analysis showed higher percentage shift in Mean Frequency of EMG towards lower frequency in the FHD group – could be an indicator of fatigue. FMS correlated best with functional disability.

CONCLUSION: These observations have important pathophysiological and therapeutic implications. They point to abnormalities in the central motor drive bilaterally, abnormal SMO and impaired inhibitory mechanisms. Combining TMS, functional imaging with EMG can characterize and delineate the basis of ontogeny further - the importance being, to see if one could devise treatment strategies like EMG guided denervation, rTMS, Bio-feedback, peripheral FES designed to ameliorate this functional disability

TABLE OF CONTENTS

INTRODUCTION

Dystonia is the term for a set of disorders characterized by involuntary sustained muscle contractions leading to abnormal postures that interfere with motor performance. **Task specific dystonias** occur during selective activities that involve highly skilled, repetitive movements. Writer's cramp (Focal Hand Dystonia) is the prototype commonest task specific dystonia characterized by heterogeneity with marked individual variability. Initially, the dystonia manifests only on performance of the specific motor task, however with progression of disease, it may occur with other tasks or even at rest. Abnormal posturing of the hand may occur as writing continues necessitating periods of rest and significant functional disability. Neurological examination is usually unremarkable.

Inspite of the remarkable strides being made into the proposed etiology and pathophysiology of this disorder; the **treatment options still remain limited and suboptimal**. The selectivity and task specificity eventually leads to frustration even necessitating change of occupation due to disability. **The need to provide a feasible and effective treatment option remains the principle focus of majority of the studies on WC.**

Surface EMG is a simple non-invasive technique to both qualitatively and quantitatively analyze the abnormalities in FHD. However, studies on the dystonia phenomenology, temporo-spatial spread of activity, EMG patterns in WC and their correlation with functional disability are relatively scarce. Integrating available data on pathogenesis like

impaired surround inhibition, abnormal Sensori-Motor Organization (SMO) and plasticity with observations from EMG analysis is likely to provide useful insights into potential therapeutic targets. This forms the basis for undertaking the study. Possible strategies having therapeutic potential include EMG guided denervation, biofeedback, peripheral Functional Electrical Stimulation (FES), rTMS and multidisciplinary approaches.

Studies will need to be further improvised for extending the benefit of outstanding research work to devise novel therapies. Joint collaboration between Biomedical Engineering and Clinical Neurophysiology will facilitate the same.

The proposed study is aimed at providing information regarding the **ontogeny, recruitment patterns and electromyographic abnormalities in Focal Hand Dystonia** and correlate these findings with the functional disability. We intend to provide a qualitative and quantitative assessment of the EMG patterns in FHD compared with controls. The study design was unique as it included:

1. inclusion of novel 16 channel EMG using surface electrodes including the normal contralateral limb
2. customized software to acquire, rectify and integrate the EMG signals for further qualitative and quantitative analysis.
3. recording done during different phases of a "writing task" which includes a paragraph as it is well known that the difficulty increases with prolonged writing. The phases include rest, preparing to write, writing and relaxation.

LITERATURE REVIEW

Historical perspective

Ramazzini provided one of the first descriptions of task-specific dystonia in 1713 in "scribes and notaries".[1] Initially attributed to overuse, subsequently to psychogenic causes because of the task-specific nature of the manifestations, relief with sensory tricks and stress induced exacerbations,[2] it was only in the 1970s that writer's cramp was recognized as a form of idiopathic dystonia related to dysfunction of the basal ganglia. Then in 1982, Sheehy and Marsden described the dystonic features in their series of patients with writer's, musician's and typist's cramp. [3]

Clinical presentation:

The usual age of onset of task-specific dystonias spans the third to sixth decade. [3, 4]

It is characterized initially by an abnormally tight grip while writing with progressive difficulty in performing the task with painless and painful hand and forearm cramping as writing continues. [5]Hand–wrist flexors are more commonly involved than extensors, even though hyperextension of the distal phalanges or even the fingers has been seen. [3] Excessive muscle spasms may progress to more proximal muscles around the elbow and shoulder, producing abduction of the arm. Sensory tricks such as rubbing the back of the hand may diminish writer's cramp. An initial classification divided the patients in two groups, simple and dystonic writer's cramp, on the basis of the absence or presence of dystonia while performing other tasks. [3] However, about half of the patients with simple cramps progress to having dystonia with other activities.

About a third of patients with writer's cramp have intermittent symptoms that are not disabling. However, the rest have constant abnormal writing that can become illegible. Remissions are uncommon, and symptoms can progress to the other hand. [3, 5, 6] Poor prognostic factors include secondary dystonia, tremor, and long-duration or progressive symptoms.[7]

Examination should include confirming task specificity, ruling out multifocal involvement, tremors, myoclonus. Ascertainment of mirror dystonia helps in identifying dystonia from adaptive/ compensatory mechanisms. [8]

EMG shows the simultaneous activation of agonist and antagonist muscles (co-contraction). The pattern is of complete lack of selectivity for individual muscles with overflow of contraction to muscles not normally activated by the task being performed. [9, 10] Further details on EMG will be mentioned in the subsequent sections. EMG is also useful as a guide to botulinum toxin injections.

ENMG studies may also help identify other peripheral nervous system abnormalities such as carpal tunnel syndrome that could be exacerbated by focal dystonia. Brain imaging for diagnostic purposes is not routinely recommended.

Differential diagnosis includes primary writing tremor, non–task-related dystonias, parkinsonism-associated dystonias, carpal tunnel syndrome, neuropathies, plexopathies, repetitive stress injury, thoracic outlet syndrome and other vascular insufficiencies, reflex sympathetic dystrophy, and psychogenic movement disorders.

Burkhe Fahn Marsden Scale [11] is used to assess clinical severity of dystonia in trials

0. No dystonia present
1. Slight dystonia. Clinically insignificant
2. Mild. Obvious dystonia, but not disabling
3. Moderate. Able to grasp, with some manual function
4. Severe. No useful grasp

Epidemiology and risk factors:

Ten to 20% of patients with task-specific dystonias have a positive family history. [12]. DYT 1, 6, 7, 13 and abnormalities linked to chromosome 18 have been implicated in some cases of task specific dystonia [13, 14, 15]. The generally accepted concept is that FHD is due to a combination of individual vulnerability and environmental factors. A recent case control study involving 104 subjects by Roze et al [16] has implicated the following risk factors:

1. Risk increased with the time spent writing each day and was also associated with an abrupt increase in the writing time during the year before onset
2. Head trauma with loss of consciousness
3. Myopia

No significant association with peripheral trauma, left-handedness, constrained writing, writing in stressful situations or the choice of writing tool was found.

A bimodal age distribution at 20 and 45 years was noted in the study. Females constituted 62% of the population in contrary to the male prominence reported in literature [2]**.** Flexion, extension and pronation/ supination were the types of writer's cramp noted commonly in the same order. Cases also had a college or university degree more frequently than controls. Sheehy et al. reported that only 5% of 91 patients with writer's cramp had a history of a hand injury in the preceding 3 months of the appearance of the dystonia. [5]

REGIONAL PATHOPHYSIOLOGY AND ANATOMICAL SUBSTRATES

Volumetric analysis have shown abnormalities in the putamen, premotor and sensorimotor cortex, thalamus and cerebellum, however data on these are conflicting. Garruax et al demonstrated significant **bilateral** increase in gray matter in the hand representation area of primary somatosensory and, to a lesser extent, primary motor cortices in 36 patients with unilateral FHD compared to controls using voxel-based morphometry. [17]. Conflicting report of gray matter decrease in the hand area of the left primary sensorimotor cortex, bilateral thalamus, and cerebellum was reported by Delmaire et al [18]

Functional neuroimaging using either positron emission tomography (PET) or functional MR imaging (fMRI) and appropriate activation procedures give useful information regarding the abnormalities. Hand movements in healthy individuals activate the contralateral primary motor and sensory cortex, ipsilateral cerebellum, premotor cortex and bilateral supplementary motor area. [19] Both hypometabolism [20] and hypermetabolism of the premotor cortex have been described. [21] Preibisch et al using functional MR

showed significantly greater activation of the ipsilateral cerebellar hemisphere, caudal and anterior extension of activation in the primary sensorimotor cortex towards the premotor association area. Activation was also observed in the thalamus during writing only among the writer's cramp group. These indicate an increased basal ganglia output via the thalamus to the motor and premotor cortical areas in dystonia patients and support the notion of disinhibition of the motor cortex leading to cocontractions and dystonic postures. [22]

In one fMRI study by Blood et al, FHD patients showed persistent elevations of basal ganglia activity even after stoppage of the finger tapping task, suggesting that this persistence could have reflected a defect in inhibitory control. [23] However, this study lacked corresponding EMG monitoring of the muscle.

Tempel et al demonstrated with blood flow scans during vibratory stimulus that there was bilateral reduction in peak responses noted from the primary somatosensory cortex and supplementary motor area. This study provided evidence for abnormal sensory motor processing in FHD. [24]

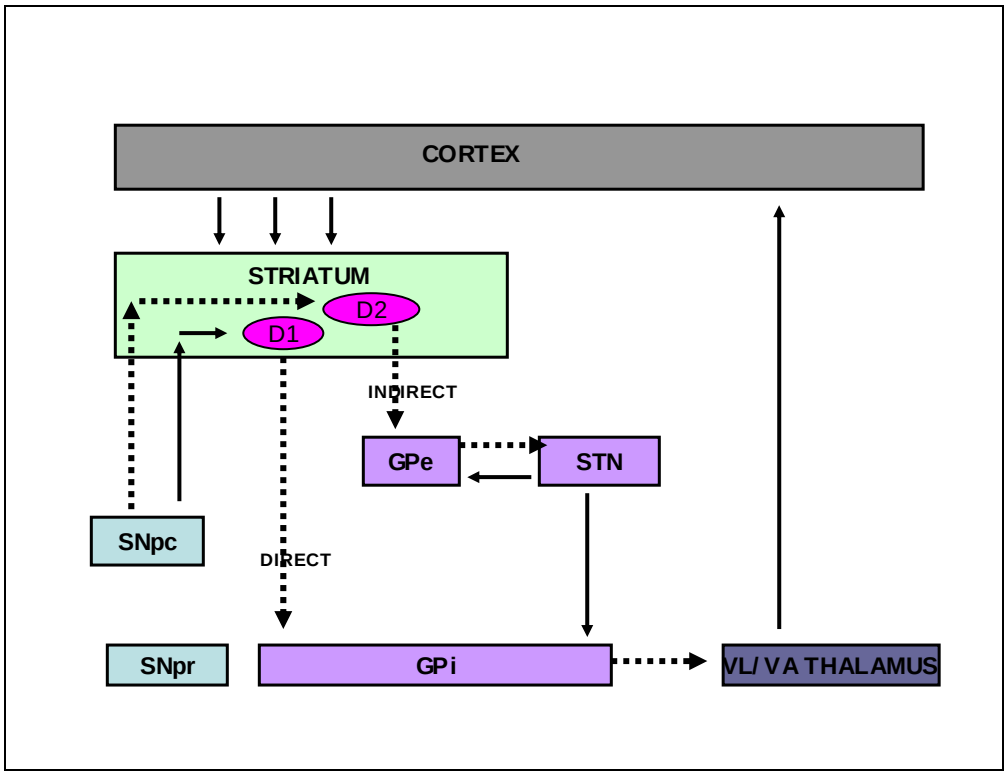
Cortical basal ganglia circuits in dystonia

Cortical motor areas (primary motor, premotor, supplementary motor and premotor areas) through direct and indirect pathways form a closed loop through the globus pallidum interna and thalamic nuclei back to the cortical level

- the indirect pathway (GABA) is faster and stronger than the direct (glutamate) striatal pathway.

- a primary function of the indirect pathway may be to broadly inhibit unwanted muscle activation during an intended movement.[25]

Figure showing Cortical – Basal Ganglia – thalamus connections (note the indirect and direct pathways)



- also, the indirect pathway projects onto the GPi (globus pallidus interna) less selectively than the direct pathway, which provides the anatomic basis for selected facilitation and surround inhibition modulated by the basal ganglia.

Inhibited indirect pathway or excessive direct pathway could lead to a decreased output from the GPi and lack of focus on motor activation.

PET measurements revealed a putaminal decrease in D2-like receptor number (by 29%) in patients with FHD. [26] A defect in GABA level in the lenticular nucleus contralateral to

the affected hand has been found in people with writer's cramp by using MR spectroscopy.[27]

While sensori-motor learning takes place, neuronal activity in striatum and pallidum have shown to reflect adaptation.

Loss of cortical control of subcortical structures can result in progressive disability in finger movement and the hand moving en bloc causing excessive grasping.

Task specificity:

The most fascinating aspect of FHD continues to be the task specificity, this aspect of the disease has received comparatively less attention. Task-specificity suggests that the underlying task (program) - to - motor output (effector) relationship is intact for many activities except writing. The specific linkage is between linkage of one motor program with an effector. The potential role of premotor cortex in this function is being evaluated currently. [28] A dysfunction of the supplementary motor area in dystonic patients has been indicated by the findings of enlarged amplitude of the 30 N component of the somatosensory evoked potential by Reilly et al.

The deficient activation of the premotor cortex in functional neuroimaging [29] substantiates the point that the area may be a site of potential overlap between the program and effector and most likely plays a role in the disordered movement.

Neurophysiological studies using transcranial magnetic stimulation (TMS) are currently underway to provide further insights into the premotor – motor cortex circuitry and somatotopy.

The physiology of task specificity in FHD has been studied with studies of the CNV (Contingent Negative Variation). The CNV is a slow negative EEG potential that arises between two stimuli triggering a reaction time movement. The first stimulus, S1, acts as a warning stimulus, and after an interval, the second stimulus, S2, "commands" the move ment. The beginning of the CNV is thought to be related to sensory processing of S1 and the end of the CNV is thought to be related to motor preparation. Hamano et al [30] showed that the FHD subjects showed normal CNV for neck movement but significantly decreased CNV amplitudes for movements both in the affected and unaffected hands. This showed abnormal motor programming including the unaffected limb as well with task specificity.

Lack of inhibition:

Lack of inhibition at multiple levels could explain the unintended activation of muscles and the resulting abnormal movements in patients with task-specific dystonia.[31] This is reflected as co-contraction and motor overflow of activity leading eventually to abnormal postures.

Facilitation of the H-reflex, indicating a disturbed reciprocal inhibition in writer's cramp, has also been detected bilaterally in subjects with FHD. [32, 33, 34]

Transcranial magnetic stimulation (TMS) studies in patients with task-specific dystonia have revealed defects consistent with reduced cortical inhibition. Short intracortical inhibition (SICI) is reduced in bilateral cortices of patients with unilateral writer's cramp, suggesting that this defect occurs in the affected and unaffected sides [24,35,36] Patients with writer's cramp also have a significant reduction of the long intracortical inhibition only in

the contralateral hemisphere and only during muscle activation.[34] Abnormal intracortical inhibition may contribute to a lack of specificity in the output from the cortex and the development of unwanted motor activation.

Surround inhibition:

The brain must activate the specific motor activity with suppression of other unwanted movements. Sohn and Hallet studied the Motor Evoked Potential (MEP) from the index and little fingers during TMS triggered by self initiated voluntary contraction of the index finger. The MEP from the little finger was enhanced in the FHD group compared to the normals who showed suppression of the little finger responses. This phenomenon seen in FHD group could be attributed to disturbed surround inhibition. [37]

Rosenkranz et al studied the pathophysiological differences between musician's and writer's cramp by using TMS. They compared the spatial pattern of sensorimotor organization in the motor cortex of these patients with healthy musicians and nonmusician control subjects using focal vibration of one hand muscle and measured the corticospinal excitability to that muscle and other hand muscles. In the vibrated muscle of healthy non-musicians, vibration increased the amplitude of the MEP and decreased the SICI. But it had the opposite effects on the other hand muscles, which could be interpreted as **focal facilitation with surround inhibition**. Vibration had little effect on patients with writer's cramp, but it reduced SICI in **all hand muscles**. In the vibrated muscle of healthy musicians, the results were intermediate between the healthy nonmusicians and the dystonic musicians. Patients with different forms of FHD share a

variety of abnormalities in sensory processing, sensorimotor organization (SMO) and motor excitability. [38]

However, the way in which SMO responds to behavioral proprioceptive training is influenced by the baseline pattern of SMO, which itself is determined by the musician's status and the presence of focal hand dystonia. Thus therapeutic paradigms that attempt to restore physiologic patterns of SMO in patients may need to be adapted to the baseline state of the individuals being treated rather than relying on observations made in healthy subjects. Further studies should address the question whether the prolonged application of behavioral proprioceptive training improves hand function in FHD.

Abnormal Plasticity:

Plasticity, or changes in how brain pathways respond to various stimuli, may contribute to the development of task-specific dystonia

Changes in the Somatosensory homunculus: The fingers of the hand are very closely spaced in this representation. Certain kinds of jobs like that of musicians, writers etc require extensive and fast use of fingers. When this continues over a long period (as long as 25 to 30 years), there is a reported 'blurring' in the homunculus in the area for fingers [39,40]. The somatosensory area for one finger slowly overlaps on that of others and so the brain cannot efficiently distinguish which finger is being controlled

Cortical TMS has provided useful insights into this phenomenon of increased plasticity. In healthy subjects, peripheral nerve stimulation increases the motor response to TMS and the motor facilitation is limited to the muscles innervated by the peripheral nerve that was stimulated. (Paired Associative Stimulation). This response is larger in patients with

task-specific dystonias and spreads to muscles not innervated by the stimulated nerve. This finding is indicator of abnormal increase in corticospinal excitability with defects leading to attenuated reinforcement of the intracortical inhibitory circuits. [41] Quartarone et al also proposed that the homeostatic mechanisms that stabilize the excitability levels within a dynamic range are impaired in FHD, the faulty homeostasis may favour maladaptive plasticity. [42]

They also suggested that repetitive skilled motor practice leads to excessive formation of associations between the sensory input and motor outputs (abnormal potentiation) and a failure to weaken existent associations (deficient depotentiation).[43] This as an environmental trigger along with a permissive state or preexisting genetic predisposition may precipitate symptoms of FHD in an individual.

Abnormal Sensori - motor integration:

FHD may have sensory abnormalities including deficient graphesthesia [44] and temporal and spatial discrimination ability [45,46]. Putzki et al noted impaired responses to passive finger movements implicating that kinesthesia are impaired in FHD. [47] Voxel-based morphometry studies in patients with focal hand dystonia show an increase in gray matter in the primary sensory cortex [17]. Reduced blood flow in the sensorimotor cortex in response to vibration has also been demonstrated. [24]

The dipoles of the N20 from stimulation of individual fingers show disordered representation in the primary sensory cortex and these abnormalities are present on both hands of patients with FHD [48]

Kaji et al demonstrated vibration induced dystonia and relief following intramuscular injection of lignocaine in FHD, the muscle spindles had a pivotal role in producing dystonia [49]

Repetitive motor activities may broaden sensory fields in the sensorimotor cortex associated with development of dystonia. fMRI studies also suggest that there may be broadened sensory fields in people with hand dystonia. Less segregation could be associated with spreading and overflow during motor activities. The scope of entraining SMO with proprioceptive training will be discussed in the subsequent section on treatment.

Studies using magnetoencephalography to evaluate sensory cortex in subjects with task-specific dystonias have shown a clear disarray of the nondystonic hand representation, another sign of endophenotypic rather than adaptive sensory dysfunction. [48] Also, reciprocal inhibition is defective on both the affected and the nonaffected arm in writer's cramp patients. [33]

In the precision hand grip experiment, FHD subjects showed shorter latency of grip force response, grip force overshoots during early lifts with subsequent adjustment to normal steady state values. These could be attributable to a "prelearned" or "anticipatory" phenomenon. [50]

A study using SEPs found impaired modulation of premovement sensory input with loss of the normal attenuation of SEPs in preparation for movement in people with writer's cramp [51] again speculating that the abnormalities may be setting in before the actual initiation of movements.

Quartarone et al also demonstrated increased MEPs from the muscles involved and even the hand and forearm muscles that were not involved during the motor imagery (mental rehearsal of a motor act without overt movement) of tonic finger movement, this again suggests increased corticospinal excitability. [52]

Abnormalities in the contralateral limb:

Abnormalities in the contra lateral normal limb have been detected in many of the studies mentioned above. The concepts of contra lateral overflow and mirror dystonia were described by Sitburana et al. [53]. Overflow is defined as unintentional contractions which accompanies, but is anatomically distinct from the primary dystonic movement.

Three different patterns of motor activity were noted:

Ipsilateral overflow: involuntary contraction of muscles adjacent to those involved in FHD (reported in 1/3rd of subjects)

Contralateral overflow: involuntary movement or dystonic posture in the normal contralateral limb during dystonic movements or posture of the hand primarily affected by FHD

Mirror movement: is described as involuntary movement in one side of the body which mirrors the voluntary movement performed in the homologous body part. (reported in 2/3 rd of the subjects)

The subjects were examined for the presence of overflow and mirror dystonia (during movement of the normal limb) during writing, drawing and performance of repetitive tasks. The presence of overflow and mirror dystonia correlated with the severity of dystonia.

Mirror dystonia is believed to occur due to simultaneous activation of crossed corticospinal pathways, mediated by altered transcallosal fibre inhibition. Merello et al described this phenomenon in 44.6% of 65 patients in his series. [54]

Electromyogram in FHD:

Cohen and Hallet had initially published the series on Electromyographic findings in hand cramps**,** 12 of the 19 subjects studied had WC. [9] They noted a relatively heterogenous spectrum. The observation of alternating agonist-antagonist muscle activation replaced by a co-contracting pattern was noted. Both short duration and long duration (more than 100 msec) bursts were noted. The different muscles activated and varied patterns were attributed to different patterns of writing (pen moved mainly by the finger movements, pen moved by wrist abductors, pen moved by action of forearm muscles, pen moved only with proximal muscles of the arm without any finger movements). The electrophysiological abnormalities were mainly noted in the first two groups.

Hughes and McLellan [10] had mentioned increased co-activation of the upper limb muscles including the triceps in his series of 11 patients with WC.

There were no reports of demonstration of the phenomenon of motor overflow or ontogeny using surface EMG recordings. The pattern of activity in the normal contralateral upper limb also is unknown.

The mirror movements have been used to identify appropriate muscles for Botox injections [2,8]

Cocontraction:

Different co-contraction patterns are noted as mentioned earlier.

Farmer et al [55] had analysed the co-contraction patterns between the healthy and dystonic subjects. They concluded that the co-contraction seen in dystonia is neurophysiologically different from voluntary co-contraction in healthy individuals and result from abnormal synchronization of presynaptic inputs to forearm antagonist muscles. The cross-correlogram from the dystonic subjects revealed broad motor unit peak synchronization and significant frequency domain coherence.

Treatment:

Pharmacological:

Anticholinergic, dopaminergic, and GABAergic medications individually and in combinations have been used empirically with some inconsistent success for generalized dystonia and severe focal dystonia. [56, 57] Although oral medications have provided benefits in selected patients, these drugs have often dose-limiting side effects.

Botulinum toxin:

Randomized, double-blind, placebo-controlled trials of BNT type A for writer's cramp have shown benefit after one or multiple injections. [58-61]. Long-term follow-up on patients with writer's cramp treated with chemodenervation were consistent with normalized writing in 46% patients, and partial benefit in another 10%, lasting a mean of 6 months after the procedure, the failure rate was 21% and loss to follow-up 23%[7] and this approach has been shown to be safe. [62] However, the main challenge is to provide

adequate benefit without loss of function associated with weakness. This requirement is particularly important in those that still expect high-level fine activity with the affected limb. Secondary dystonia, tremulous WC, long duration WC and progressive WC were associated with poor outcome. [7]

BNT may block gamma motor neurons preferentially over the alpha motor neurons, decreasing the muscle activity on the spindle more than the extrafusal fibers. This mechanism may explain how BNT can alleviate excessive contraction without causing weakness. Priori et al identified increment in the second phase of reciprocal inhibition by studying the H reflex of the forearm flexors in dystonic subjects after injection of botulinum toxin. [63] There was also a study by Gilio et al who postulated effects of the botulinum toxin on intracortical inhibition, the quantification was done using transcranial magnetic and EMG studies. [64] Ceballos-Baumann showed that in contrast to the clinical response, botulinum toxin did not reverse the associated dysfunction in the primary motor and premotor cortex using PET studies. [65]

Surgery:

Taira et al reported disappearance of dystonic symptoms after stereotactic nucleus ventrooralis thalamotomy in 12 patients with FHD over a mean followup of 13.1 months[66]

Deep brain stimulation of the thalamic Ventro-oralis complex is also being considered a useful neurosurgical option in severe dystonias. [67]

Rehabilitation strategies:

Specially designed splints or thicker pens may help writer's cramp.

Sensory motor retuning: based on principle of plasticity. It has been thought that by immobilizing the dystonic limb one could reverse the abnormal sensorimotor pattern, helping reduce focal dystonia symptoms. This approach has provided some benefit to task-specific dystonia patients after immobilization for a mean of 4.5 weeks.[68] Benefit persisted in most patients after 20 weeks, but longer-term follow-up and cost-effectiveness analysis of the immobilization have not been reported.

Byl et al.[44] have shown that sensory retraining, nonstressful hand rehabilitation, and other nonpharmacological techniques can be useful in patients with task-specific dystonias

However, studies with a large patient base, with long-term benefit ascertainment, controlled, and under blinded assessments are lacking.

Individual fingers practice writing with finger pens while the other fingers are splinted

Based on concept of abnormal sensory function: training each individual finger to read Braille for 30-60 minutes daily can lead to improved sensory discrimination and improved motor function with improvement in dystonia severity scale and reduced time for writing. [69, 70]

Injection of dilute lidocaine into muscle preferentially blocks the gamma efferents causing a decrease in spindle afferent discharge

If there is abnormal homeostatic plasticity, there would be a drive to the abnormal state again. On the other hand, since it takes many years to develop the disorder, it may require many years of rehabilitation to lead to a more permanent outcomes.

Adaptive strategies using writing device have been found useful in WC as well as primary writing tremor [71]

Since, even a multidisciplinary treatment does not alleviate the functional disability, there is a definite need to improve the knowledge regarding the physiological mal-adaptation, resulting from an abnormal sensori-motor integration in patients with FHD. In order to help address this issue, we decided to look at this disorder by making a 16 channel EMG recording system and using an electronic writing tablet with a stylus and look at the ontogeny of muscle contraction, and hence this study.

AIMS AND OBJECTIVES

EMG was recorded during different stages of a "writing task" from subjects diagnosed to have Focal hand dystonia (FHD) and normative controls. The primary aim and objectives of the study were:

1. To study the ontogeny, recruitment pattern and spread of flow of muscle contractions using surface EMG recordings in the distal, intermediate and proximal group of muscles in both the upper limbs
2. To obtain rectified mean amplitudes from all the group of muscles and compare the data between FHD subjects and controls
3. To correlate these parameters with disease severity and functional disability

The EMG recordings were obtained using surface electrodes from 4 pairs of muscles in both the upper limbs. The data were recorded and analyzed using customized software. (Further details provided in Methodology).

The data recording during the "Writing Task" included:

a. rest record
b. read the paragraph/ think and imagine writing
c. start writing
d. stop writing and relax

MATERIALS AND METHODS

DATA COLLECTION:

SUBJECTS:

Subjects attending the Neurology Outpatient Department, Christian Medical College, Vellore and diagnosed to have Focal Hand Dystonia (FHD) were recruited in the study. The study design was a prospective observational study. Normal healthy individuals in the same age group were taken as controls. The study protocol was approved by the Institutional Review Board (IRB) of the institution.

Inclusion Criteria:

1. above age 18 years
2. should have a basic knowledge of English as the writing task is in English

Exclusion criteria:

1. motor or sensory deficits due to Central or peripheral pathology
2. neurodegenerative disorders including Parkinson's disease
3. small joint arthritis
4. subjects with secondary dystonia

The aspects of electrode placement and data collection during the "writing task" were explained to the subject and informed consent was obtained. The details were collected in a standardized questionnaire. (Annexure)

The FHD subjects were graded according to **Burke – Fahn - Marden scale (BFMS/ FMS)**. It is a good index of severity of dystonia as well as the functional disability. The grading system is as follows:

0. No dystonia present
1. Slight dystonia. Clinically insignificant
2 Mild. Obvious dystonia, but not disabling
3 Moderate. Able to grasp, with some manual function
4 Severe. No useful grasp

The baseline characteristics included: age, sex, educational and occupational status, duration of illness, symptoms, clinical signs, treatment details, FM scale.

EXPERIMENTAL SET UP

Surface Electrodes:

Surface electrodes made of Ag/ AgCl were placed for obtaining surface EMG. The 4 pairs of electrodes were placed over both the upper limbs. The muscle pairs selected were:

1. Abductor Pollicis Brevis (APB) – Adductor Pollicis (ADP)
2. Flexor Digitorum Superficialis (FDS) – Extensor Digitorum Communis (EDC)
3. Biceps (BIC) – Triceps (TRIC)
4. Sternocleidomastoid (SCM) – Trapezius (TRPZ).

Circular surface electrodes of 1 cm diameter were used for hand and forearm muscle groups, electrodes of 1.5 cm were used for the larger arm and shoulder-neck muscles. The electrodes were in bipolar configuration with the discs being separated by a distance 1.5 times their diameter with an ethaflex material backing holding them at fixed separation. The surface electrodes were connected to the preamplifier with a gain of 200. The signals acquired by the electrodes were band passed between 15 and 500 HZ by the preamplifier.

EMG Preamplifier design:

The pre-amplifier gives a gain of 200 to the signals from the electrodes and also incorporates band pass filtering between 15 and 500 Hz. Most of the EMG obtained during the activity of writing lies in this frequency range. The IC used here is the 8 – pin SMD type Instrumentation amplifier INA 326.

The R1 – C1 combination acts as a High Pass Filter. The cut-off frequency (fc) of the High Pass Filter is given by the equation $fc = 1/2\pi RC$.

Taking R1 = 10 KΩ and C1 = 1 μF, **fc = 16 Hz**

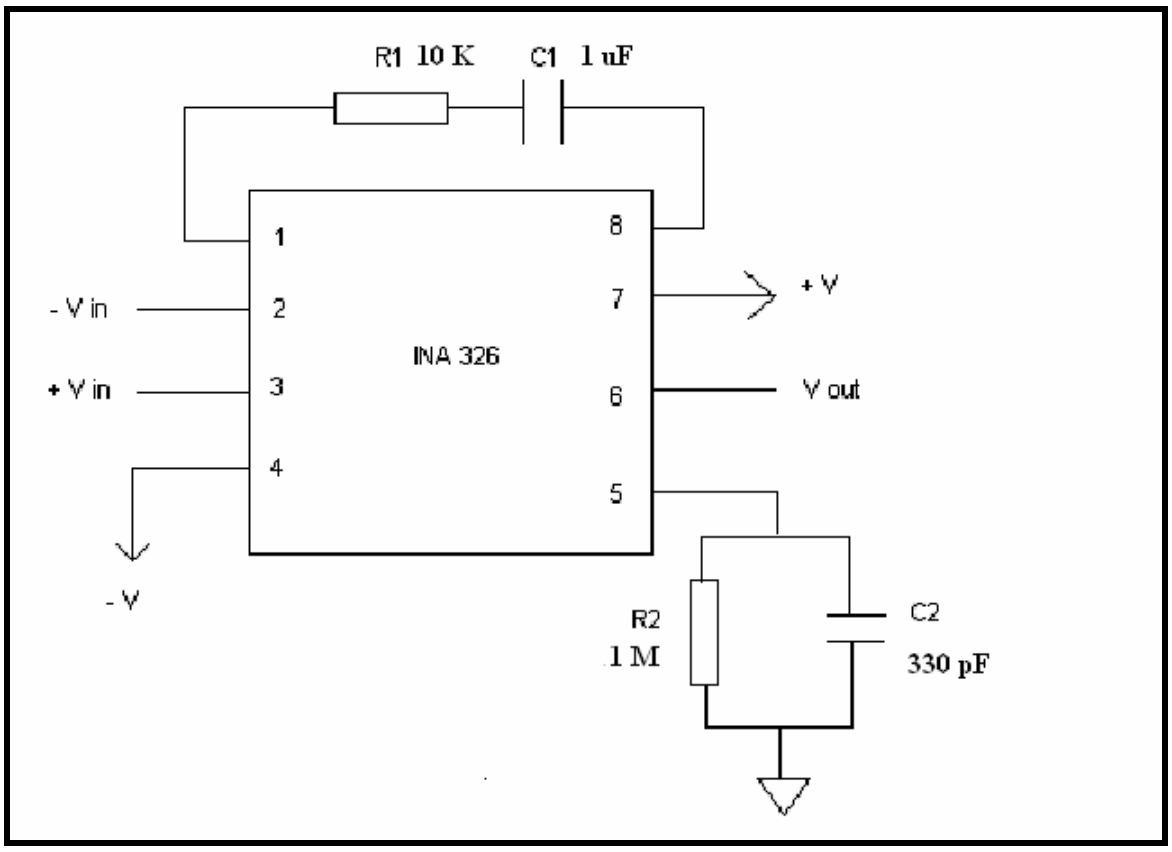
The R2 – C2 combination acts as a Low Pass Filter. The cut – off frequency of the Low Pass Filter is given by the equation $fc = 1/2\pi RC$.

Taking R2 = 1 MΩ and C2 = 330 pF, **fc = 485 Hz**

Gain = 2 R2/R1 = 200

The two filters jointly form a band pass filter for a frequency range of 16 to 485 Hz. The signal from the preamplifier is then fed to a second gain stage, where gains of 1, 3 or 10

can be selected. The overall gain could therefore be 200, 600 or 2000. During data collection an overall gain of 600 was constantly used.



Preamplifier circuit diagram

Writing tablet:

The writing tablet is one of the integral parts of the set – up. A commercially available writing tablet – G-Note 7000 V2 is used. It has a 8.5”x11”working pad, suitable for A4 paper. There is a commercial writing stylus attached to this writing tablet, which is powered by a battery. The writing tablet is powered by an internally built battery or from the computer through the USB connector.

The hand writing was recorded using a Java program which captures the X-Y co-ordinates of the stylus and the time at each co-ordinate. These values are continuously

saved in a file in the hard disk of the computer. The X-Y values are connected on screen during recording for viewing the recorded handwriting. The stylus also has a ball point tip to show the writing on the paper; this makes writing similar to natural writing on paper. When the writing tablet is connected to the computer and the program activated, the operating system 'considers' the writing tablet as a mouse. Hence, whatever is written over the writing tablet is recorded in the recording applet that is generated at the activation of the program.

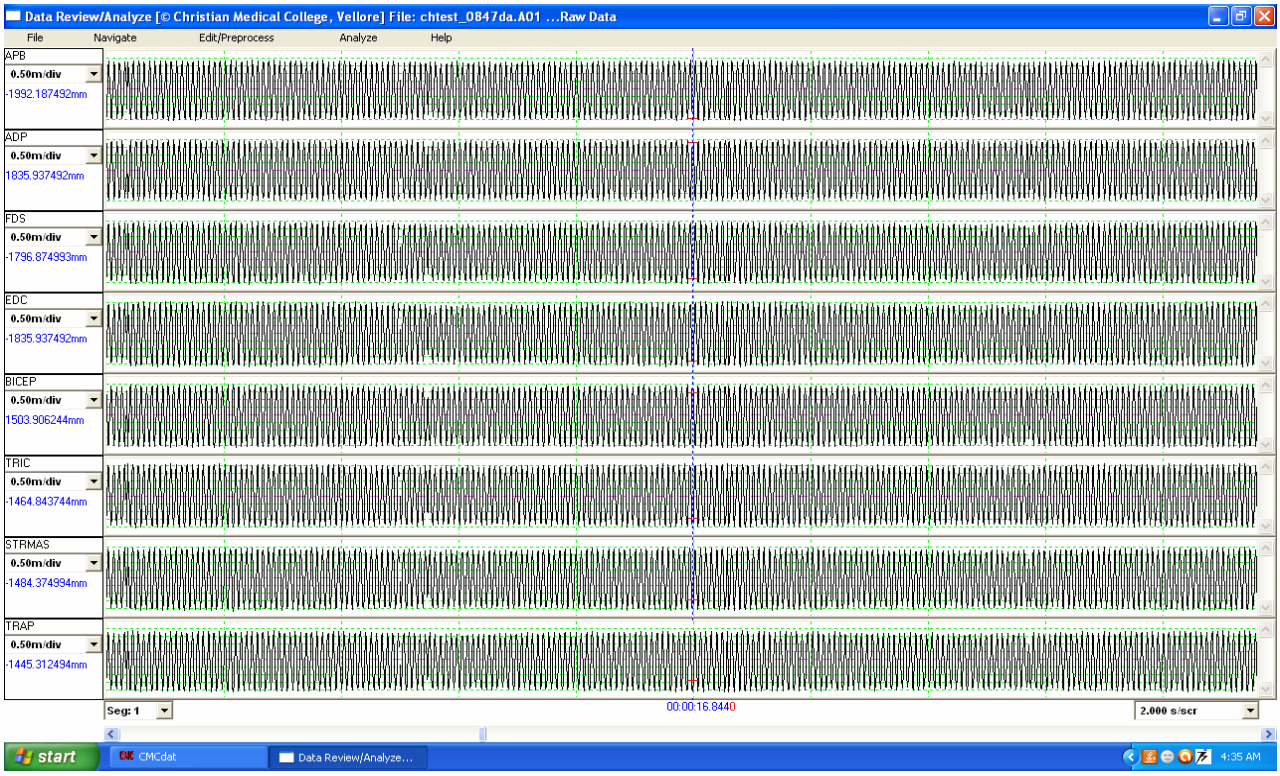
Software for EMG recording and analysis

The software for recording and analysis of electrophysiological data like EMG, named CMCDat, has already been developed in the Department of Bioengineering. Data can be recorded in a maximum of 8 channels using the software. Two separate data acquisition hardware were used. The recording can be seen as two sets of 8 – channel recordings, one for each upper limb. There are options to set the sampling rate, speed of recording, type of data whether analog or digital in the software as well as to input the short details of the experiment (experiment ID, comment box etc.). Each channel of EMG was sampled at 1000 Hz, as the EMG was band limited below 500 Hz..

Calibration of the recordings

The eight channels of the each hardware were applied a known sinusoidal voltage (4mV p-p, 100 Hz) and ensured that for the set gain the data is correctly displayed on the screen. The channels were calibrated to record amplitudes between +2.5 mV and -2.5 mV (5 mV p-p) for a gain of 600 (which was not changed all throughout the recordings and

between recordings). The following figure is that of the recording window during calibration:



Data collection:

Data collection was done in the EMG lab in the Department of Neurosciences. It is done in a cool room to minimize sweating, which otherwise can lead to electrode displacements.

Fixing the electrodes:

The site of electrode placement is cleaned with surgical spirit. The bipolar electrodes were placed over the respective muscles after applying '10-20' electrode gel. Surgical tapes were used to fix the electrode. In the palm, adhesive plaster was used to secure the electrodes. Total of 8 pairs of bipolar electrodes were used, 4 in each upper limb.

Writing task:

After fixing the electrodes, the data acquisition is started. The eight channels of data from each limb (total 16) can be seen on the computer during the recording. The non-writing upper limb is rested on a support/ table and relaxation is ensured. Once all the channels are checked for correct data, diskwriting is started and the time is noted. The **EMG is recorded throughout the duration of the entire writing task**. Meanwhile, the applet for recording the writing on the screen is also activated.

1. The subjects are asked to relax and the resting EMG is acquired for 1 minute.
2. The subjects are given a standard paragraph towards the end of this time.
3. They are asked to read it for about a minute, imagine writing and get ready for starting to write.
4. The subject is asked to copy the paragraph to the paper placed on the applet.
5. At the end of writing, he is asked to release the pen and relax, the data collection is continued for further one- two minutes.
6. The diskwriting is stopped and the electrodes are removed.

Meanwhile, the time points corresponding to the X-Y coordinates of what is being written is written simultaneously into a text file which is stored in the hard disk of the computer. In 6 FHD subjects, EMG recordings were also obtained during the process of writing on a slant board. These data were recorded for further comparison.

The subjects were given a paragraph taken from the story - 'Swami and his Friends' by R. K. Narayan, which is as follows:

" It was monday morning. Swaminathan was reluctant to open his eyes. He considered monday especially unpleasant in the calendar. After the delicious freedom of saturday and sunday, it was difficult to get into the monday mood of work and discipline. He shuddered at then very thought of school; that dismal yellow building, the fire eyed teacher and the headmaster with the long cane. By eight, he was at his desk in his room, which was only a corner in his father's dressing room. He had a table on which all his things and books were thrown in a confused heap."

This paragraph consists of few words that are not easy to comprehend. This may initiate psychological stress in FHD subjects which can potentially aggravate the disability.

DATA ANALYSIS:

Using the 'Edit / preprocess' option in the software, the raw EMG is digitally band pass filtered between 30 and 400 Hz, and notch filtered at 50 Hz. The Rectified Means of the EMG in all the 16 channels are calculated using the 'Analyze' option in the software. The absolute value of the data is taken and mean calculated. An averaging window of 400 ms was used; with the sampling frequency of 1000 Hz, the averaging window corresponds to 400 samples. The variations in amplitudes for each channel for each minute of writing were found out. This is done by generating a data file containing all the time points along with the amplitudes in each channel

(option available in the software), exporting it to a Excel spreadsheet; finding the mean and standard deviations of amplitudes in each channel.

The data is also meticulously reviewed to observe the ontogeny, patterns of recruitment and flow of muscle activity during each stage of the writing task. The recording from the normal upper limb is also reviewed to look for any contractions or mirror movements

- **Muscle activity "onset**" determination was made by careful visual inspection. Beginning of EMG activity was the point where there was significant departure from the baseline. Muscle activation time was referenced to the time of activation of APB and EMG onset times of other muscles were determined relative to the same.

- Contralateral limb activity was identified by the presence of **"coherent EMG activity"** in the contralateral limb during the performance of the writing task.

-Co-contraction was identified by the presence of **"synchronized"** contraction and relaxation in the agonist-antagonist pair of muscles.

- The functional disability of the subjects is determined based on the writing speed and legibility scores. The writing speed was considered significantly impaired if > 7 minutes (i.e more than twice the mean writing speed of the controls). Legibility scoring was done according to the following standardized scoring system: [72]

1. illegible (most or all words impossible to identify)
2. most words are illegible, meaning of the whole unclear
3. some words illegible, but the report can be understood
4. legible (all words clear)

STATISTICAL ANALYSIS:

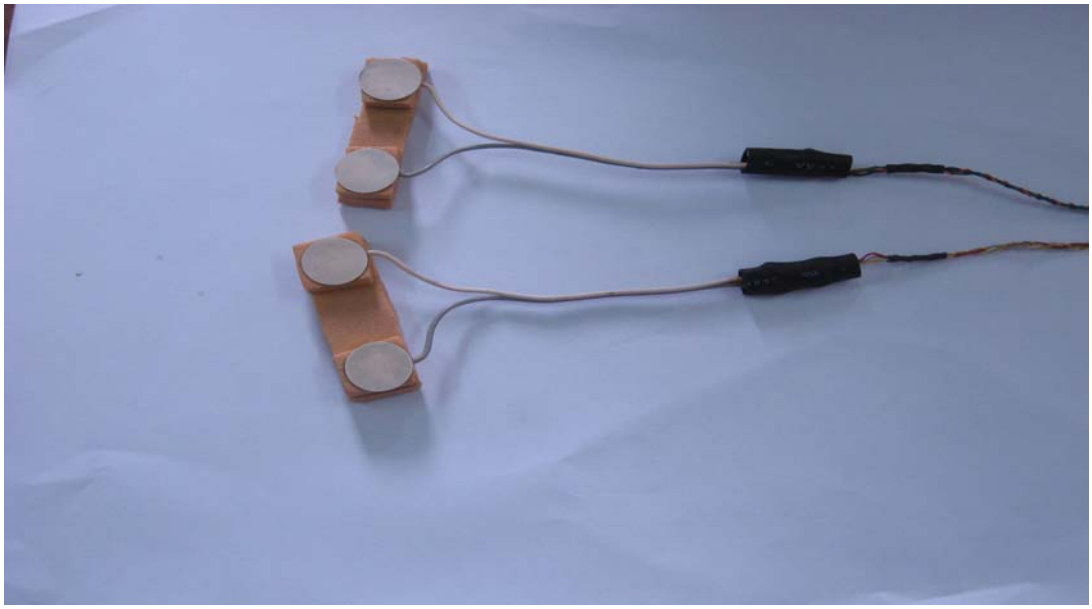
All data including the baseline characteristics, categorical variables like presence of anticipation, co-contraction, details of ontogeny and rectified SEMG amplitudes were entered into **SPSS** (version 15 for Windows). The mean amplitudes and standard deviation for each muscle during the entire writing task was calculated for both the study groups.

For variables following a normal distribution, the **unpaired t-test** was used to compare the two study group means. **Chi-square test** was done for categorical variables for testing the association with severity of dystonia and duration of illness. Probability value (p value) less than 0.05 was considered statistically significant. **Paired t-test** was used to compare the mean amplitudes of normal writing with slant board writing in the same study group to look for any differences.

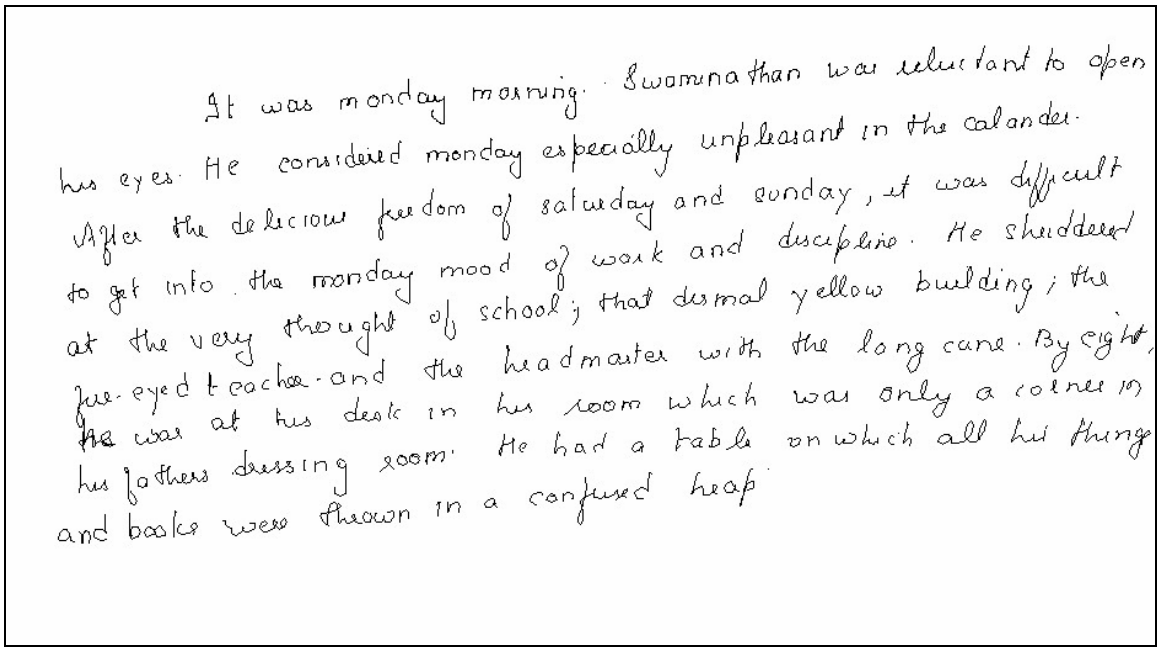
For non- parametric variables, the **Mann-Whitney test** was used for group comparisons. The mean composite end point of impaired writing speed and poor legibility score was taken as the dependent variable for assessing the predictors for functional disability using the **logistic regression** test.

WRITING TABLET WITH STYLUS

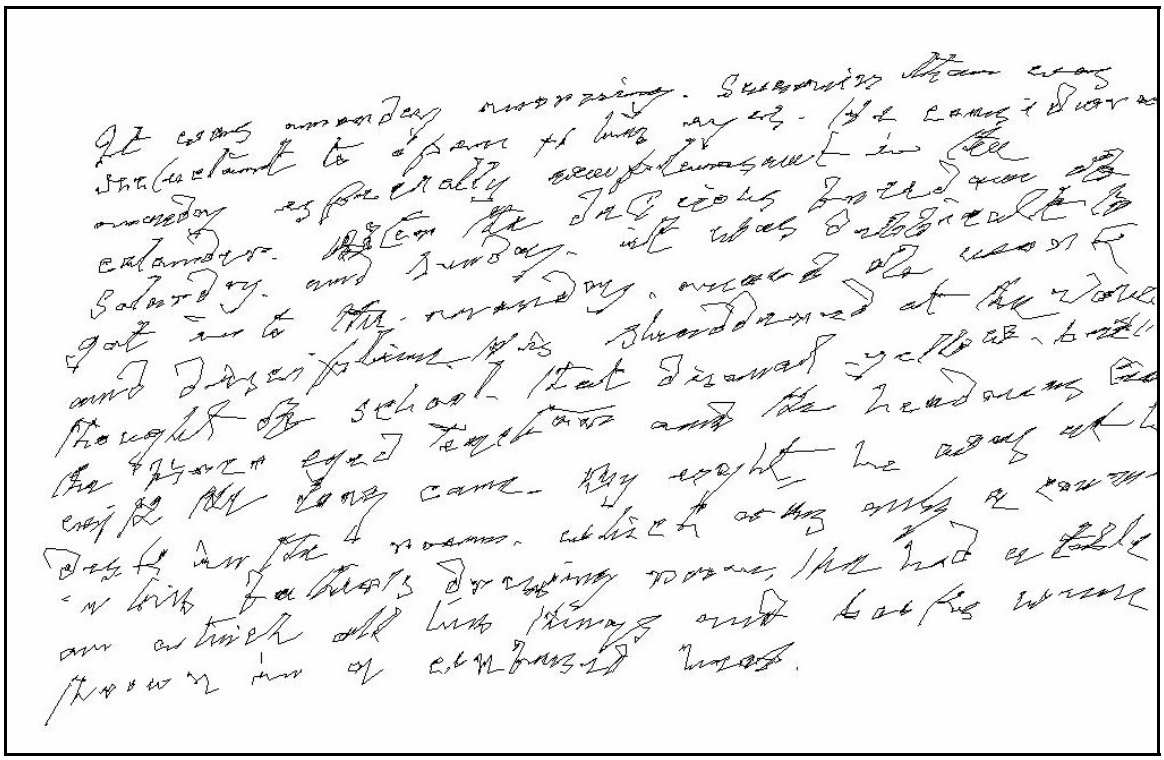
SURFACE ELECTRODES WITH PREAMPLIFIER



HANDWRITING – NORMAL SUBJECT



HANDWRITING - DYSTONIC SUBJECT



RESULTS

Data was collected from a total of 36 subjects. This included 20 subjects (18 males, 2 females) with focal hand dystonia and 16 normative controls (14 males, 2 females) belonging to the same age category. All the study subjects were right handed and the FHD group was symptomatic on the right side. The baseline characteristics of the study population are as follows:

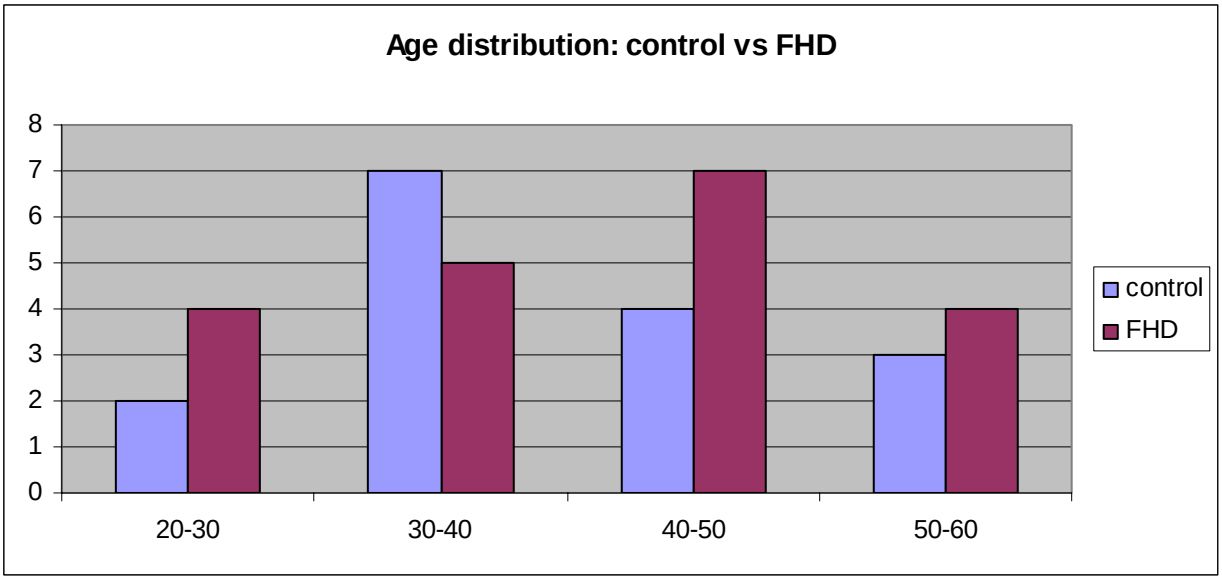
Baseline characteristics:

Age :

FHD group: mean 40.8 years, S.D 11.7 years, Range (20-60 years)

Control group: mean 40.18 years, S.D 10.8 years, Range (26-57 years)

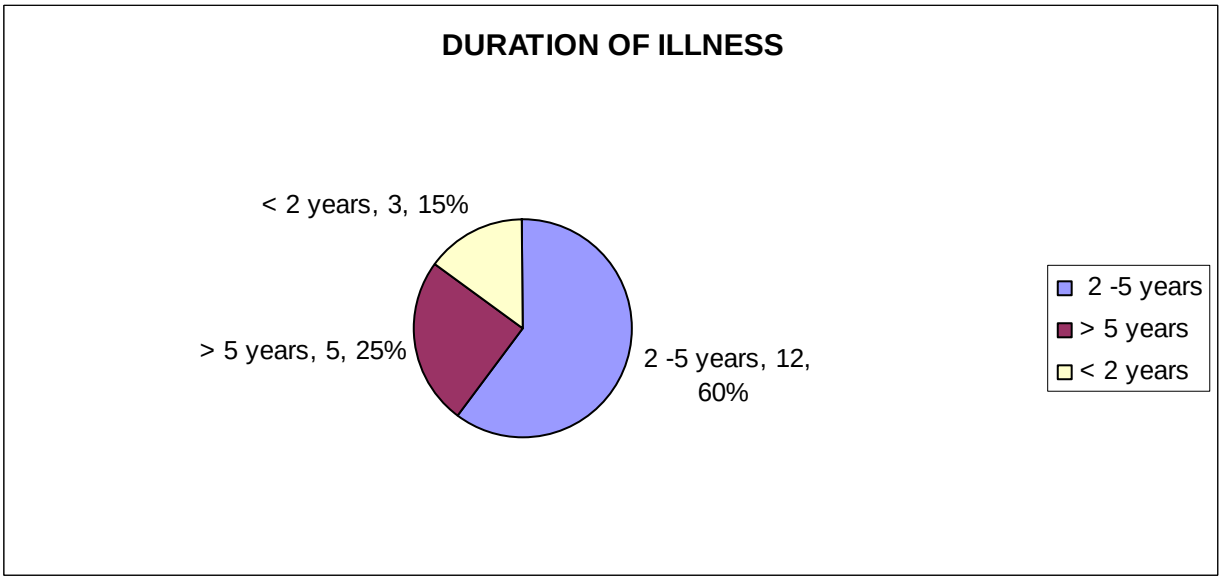
Figure 1: Bar chart showing age distribution of the two groups



Duration of illness:

Mean duration of illness prior to study: 5.23 years, SD: 3.18, Range: 1 – 12 years

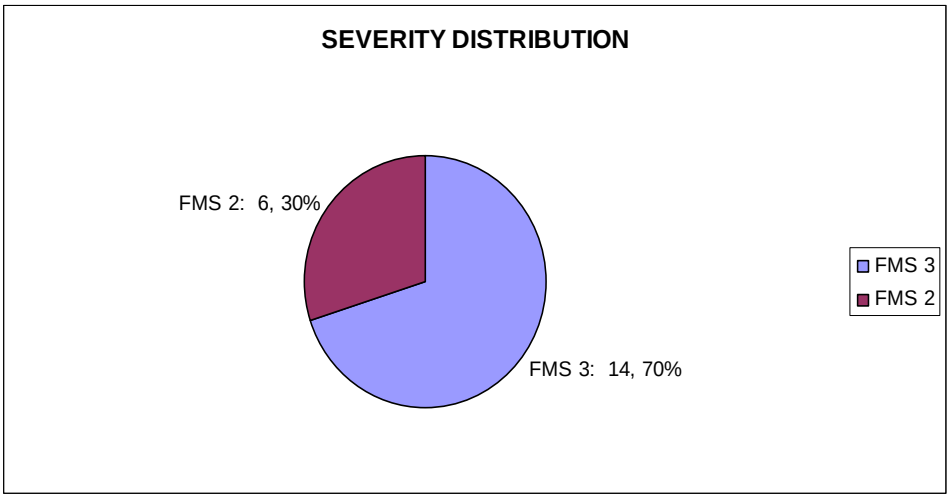
Figure 2: duration of illness illustrated on a pie-chart



Fahn Marsden scale:

- Scale 2 (mild dystonia, obvious : not disabling): 6 subjects
- Scale 3 (moderate dystonia, able to grasp with some manual function): 14 subjects

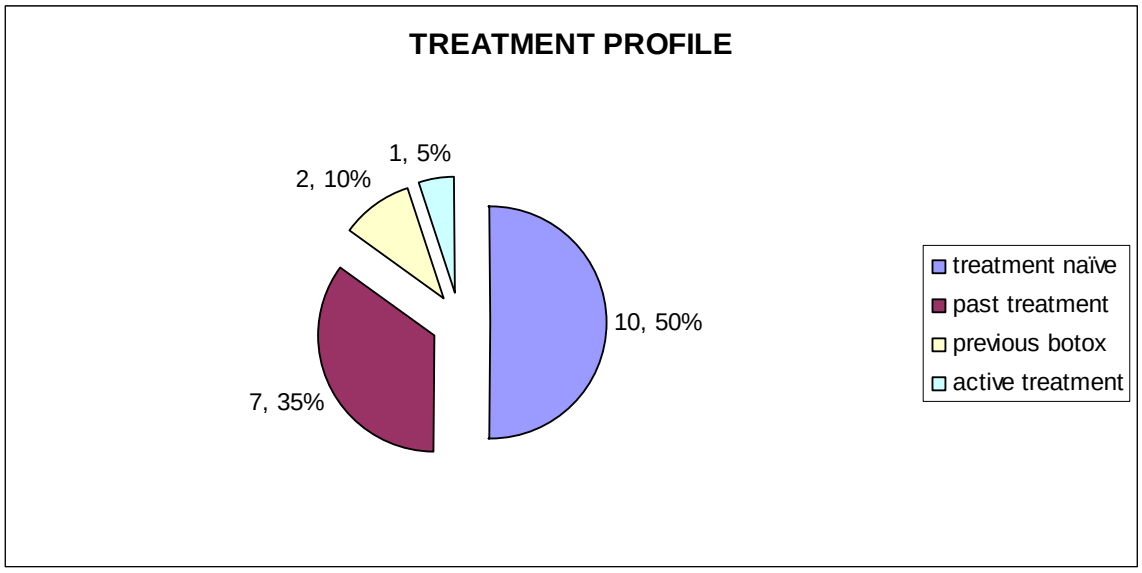
Figure 3: pie-chart showing distribution of severity of dystonia



Treatment details:

Ten subjects were treatment naïve (50%). Seven subjects had discontinued treatment (reporting suboptimal benefit). Of them, 4 had received triple therapy (Dopa depletor, anticholinergic, benzodiazepine), 2 had received benzodiazepine alone and one had received anticholinergics alone. Mean duration of discontinuation of treatment prior to the recording was 1.57 years (range: 3 days – 5 years). Two subjects had received botox injection single sitting, one in forearm flexor (one year ago) and one in the forearm extensor (2 years ago). They reported transient benefit with the same. One subject was on triple therapy and had taken medications till the day of the recording.

Figure 4: treatment profile of FHD subjects

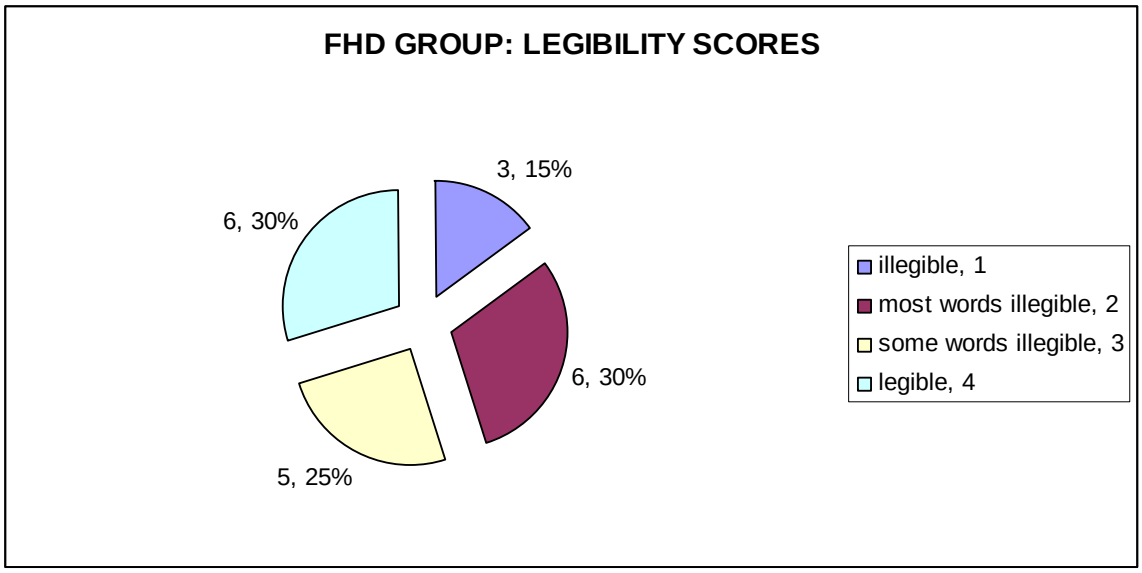


Functional disability and Legibility scores:

Mean duration to complete writing alone was 8.6 minutes (SD 3.7 minutes). Eleven of them (55%) required more than 7 minutes for writing. Posturing at the wrist and fingers were noted while writing in four subjects. Seven of them complained of severe pain while writing, this pain was localized to the hand in three, forearm in two and arm/ shoulder in one each.

The legibility scores as evaluated by two independent observers blinded to the study subjects were as given below:

Figure 5: legibility scores of FHD subjects



TIME TAKEN FOR WRITING:

Control group:

Mean time taken for completion of writing: 3 minutes 25.4 seconds,

SD: 36.8 seconds

FHD group:

Mean time taken for completion of writing : 8 minutes 6.2 seconds,

SD: 3 minutes 7.5 seconds

This is more than double the time taken for the controls. This difference in mean writing times is statistically significant (p value: 0.0001, 95% confidence interval: 183.8 - 377.8 seconds).

FHD subjects with moderate- severe dystonia (Fahn Marsden scale 3) were more likely to require more time for writing. (OR 3, CI 1.01 – 9.3, p value 0.001)

ACTIVITY OF INDIVIDUAL MUSCLES:

The activity of each muscle during different frames of the writing task was determined using rectified EMG. The mean rectified SEMG for each muscle for the normal and FHD groups are as given in the subsequent tables. A plot showing the rectified mean during the course of the writing task has also been provided. A comparison between the two graphs has been mentioned.

Figure 6: Rectified mean amplitudes (μV) during the entire writing task in controls

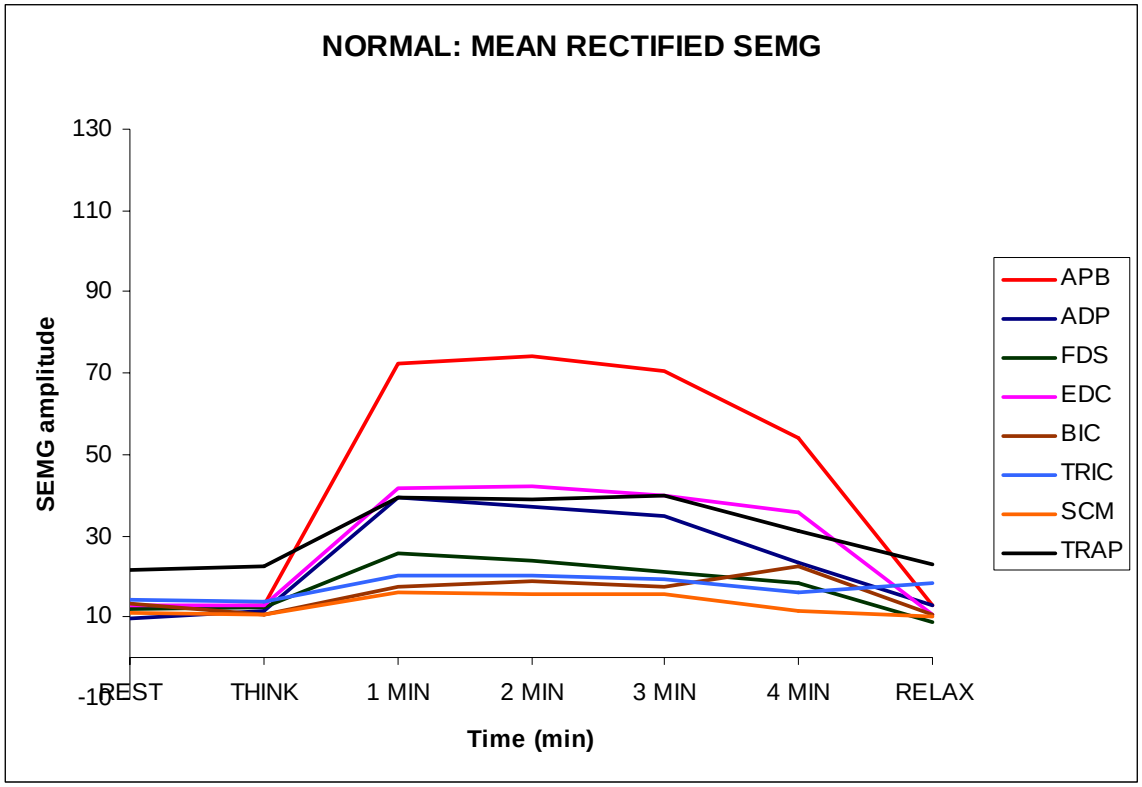
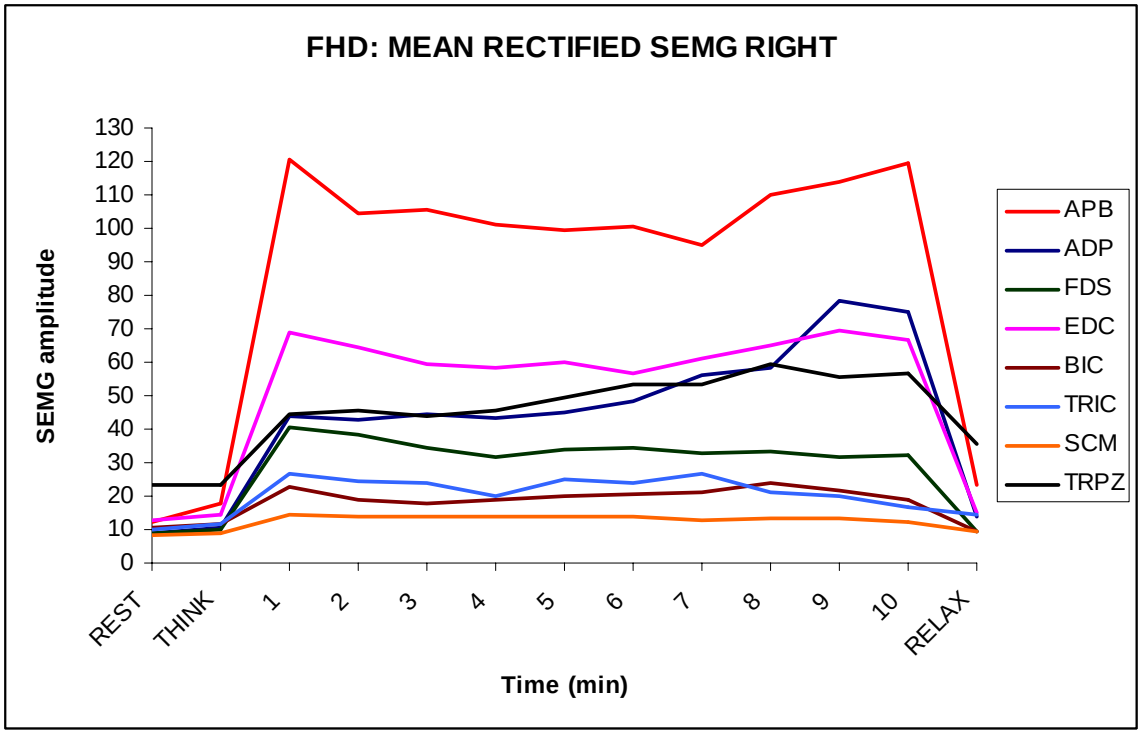


Figure 7: Mean rectified SEMG (μV) during the writing task in FHD



The salient differences between the two plots include:

1. higher amplitudes throughout the phases of writing in the FHD group noted in most of the muscles.
2. the presence of "secondary peaks" in the FHD group, ADP shows "late peaking".
3. initiation of EMG activity during the phase of thinking itself in the FHD group suggestive of "anticipation" and "early onset".
4. the SEMG amplitudes even after end of writing and during relaxation do not touch the baseline for certain muscles in the FHD group (include APB, ADP, EDC and trapezius) suggestive of "delayed offset".

Table 1: Mean Rectified SEMG (μV) for controls during the writing task

		APB	ADP	FDS	EDC	BIC	TRIC	SCM	TRP
REST	**MEAN**	12.58	9.71	12.10	12.74	13.25	14.05	10.94	21.62
	SD	4.88	5.73	10.19	6.49	11.55	6.74	5.44	13.44
THINK	**MEAN**	12.72	11.45	12.31	12.86	10.36	13.92	10.64	22.69
	SD	5.86	7.25	10.37	6.51	4.40	5.97	5.42	13.19
1 MIN	**MEAN**	72.20	39.59	25.86	41.71	17.63	20.21	15.98	39.25
	SD	48.78	18.80	11.29	14.05	9.73	7.65	16.87	24.51
2 MIN	**MEAN**	74.33	36.92	24.05	42.05	18.68	20.01	15.64	38.87
	SD	44.01	15.89	7.47	16.04	8.62	6.12	14.30	22.27
3 MIN	**MEAN**	70.73	34.78	21.19	39.73	17.65	19.12	15.68	39.96
	SD	40.92	15.66	5.84	14.37	8.31	6.54	16.87	25.15
4 MIN	**MEAN**	54	23.31	18.53	35.85	22.31	15.91	11.61	31.01
	SD	19.56	12.14	4.50	16.65	10.77	4.22	2.21	14.68
RELAX	**MEAN**	12.83	12.88	8.59	10.53	10.58	17.32	9.92	22.97
	SD	6.24	8.41	2.39	3.59	2.69	6.15	1.58	13.90

Table 2: Mean rectified SEMG (μV) in the FHD group

		APB	ADP	FDS	EDC	BIC	TRIC	SCM	TRP
REST	**MEAN**	12.28	8.79	8.62	13.02	10.77	10.17	8.15	23.53
	SD	4.89	7.48	3.31	6.78	8.50	4.36	1.92	19.84
THINK	**MEAN**	17.62	10.58	9.90	14.59	11.70	11.84	8.95	23.39
	SD	7.45	8.06	4.40	6.84	8.65	7.76	2.50	17.16
1 MINUTE	**MEAN**	120.33	43.72	40.71	68.74	21.51	26.41	14.31	44.34
	SD	55.64	22.01	19.09	29.82	13.40	17.97	8.66	20.68
2 MINUTE	**MEAN**	104.40	42.71	38.11	64.16	18.92	24.7	13.94	45.39
	SD	48.75	22.90	17.85	26.18	12.50	13.89	7.55	22.97
3 MINUTE	**MEAN**	105.62	44.67	34.27	59.21	17.83	23.98	13.73	43.68
	SD	49.83	25.92	15.69	25.29	9.60	15.84	7.84	21.47
4 MINUTE	**MEAN**	101.02	43.48	31.87	58.24	18.64	19.95	13.84	45.76
	SD	45.56	26.07	13.29	26.08	11.60	8.59	8.17	21.64
5 MINUTE	**MEAN**	99.32	44.78	33.77	60.19	20.24	24.93	13.76	49.22
	SD	49.32	26.77	17.11	31.13	14.38	22.54	8.42	22.15
6 MINUTE	**MEAN**	100.75	48.54	34.29	56.71	20.63	23.89	14.02	53.35
	SD	52.88	25.96	18.27	27.01	11.35	16.36	7.87	25.68
7 MINUTE	**MEAN**	95.10	55.98	32.94	61.10	21.22	26.55	12.99	53.44
	SD	45.03	29.31	15.72	26.08	11.13	20.78	5.71	25.13
8 MINUTE	**MEAN**	110.08	58.51	33.08	65.22	23.90	21.36	13.41	59.67
	SD	55.51	30.35	21.80	23.70	14.27	7.90	6.91	26.13
9 MINUTE	**MEAN**	113.63	78.45	31.84	69.19	21.66	20.23	13.36	55.69
	SD	57.93	40.83	14.28	24.43	10.90	7.53	6.34	29.15
10 MINUTE	**MEAN**	119.36	74.84	32.46	66.73	18.90	16.72	12.16	56.56
	SD	62.67	49.29	17.63	23.72	10.14	5.66	4.51	28.50
RELAX	**MEAN**	23.28	13.91	9.23	15.04	9.58	14.60	9.17	35.48
	SD	19.48	10.16	3.65	7.13	3.23	10.33	2.36	24.02

COMPARISON OF RECTIFIED MEAN BETWEEN TWO GROUPS:

The comparison between the rectified mean of the two groups over different time frames of writing was done using unpaired 't' test for independent samples. Mann Whitney test was used for non-parametric data wherever applicable. The analysis was as follows:

AT REST:

Table 3: comparison of resting mean SEMG amplitudes

Muscle Mean (μV) SD	Normal	FHD	p value
APB	12.58 4.88.	12.28 4.89	0.86
ADP	9.71 5.73	8.79 7.48	0.17
FDS	12.10 10.19	8.62 3.31	0.67
EDC	12.74 6.49	13.02 6.78	0.9
BIC	13.25 11.55	10.77 8.50	0.13
TRIC	14.05 6.74	10.17 4.36	0.10
SCM	10.94 5.44	8.15 1.92	0.10
TRPZ	21.62 13.44	23.53 19.84	0.87

No significant differences were noted between the two groups were noted. The baseline rest amplitudes were hence comparable. An interesting observation was that the TRPZ amplitude was higher among both the groups compared to the other muscles. This was

noted in 4 controls and 8 FHD subjects. 70% of these individuals were more than 40 years old. There was an association between age more than 40 years and TRPZ amplitude more than 20 μV (OR 2, CI 0.73-5.47, p 0.15). The other explanation could be related to larger muscle bulk and higher recruitment, the relationship in such cases can be non-linear with amplitude of EMG signal increasing greater than the actual force. It is important to note that the EMG recording was scrutinized to rule out the possibility of noise content overlapping EMG.

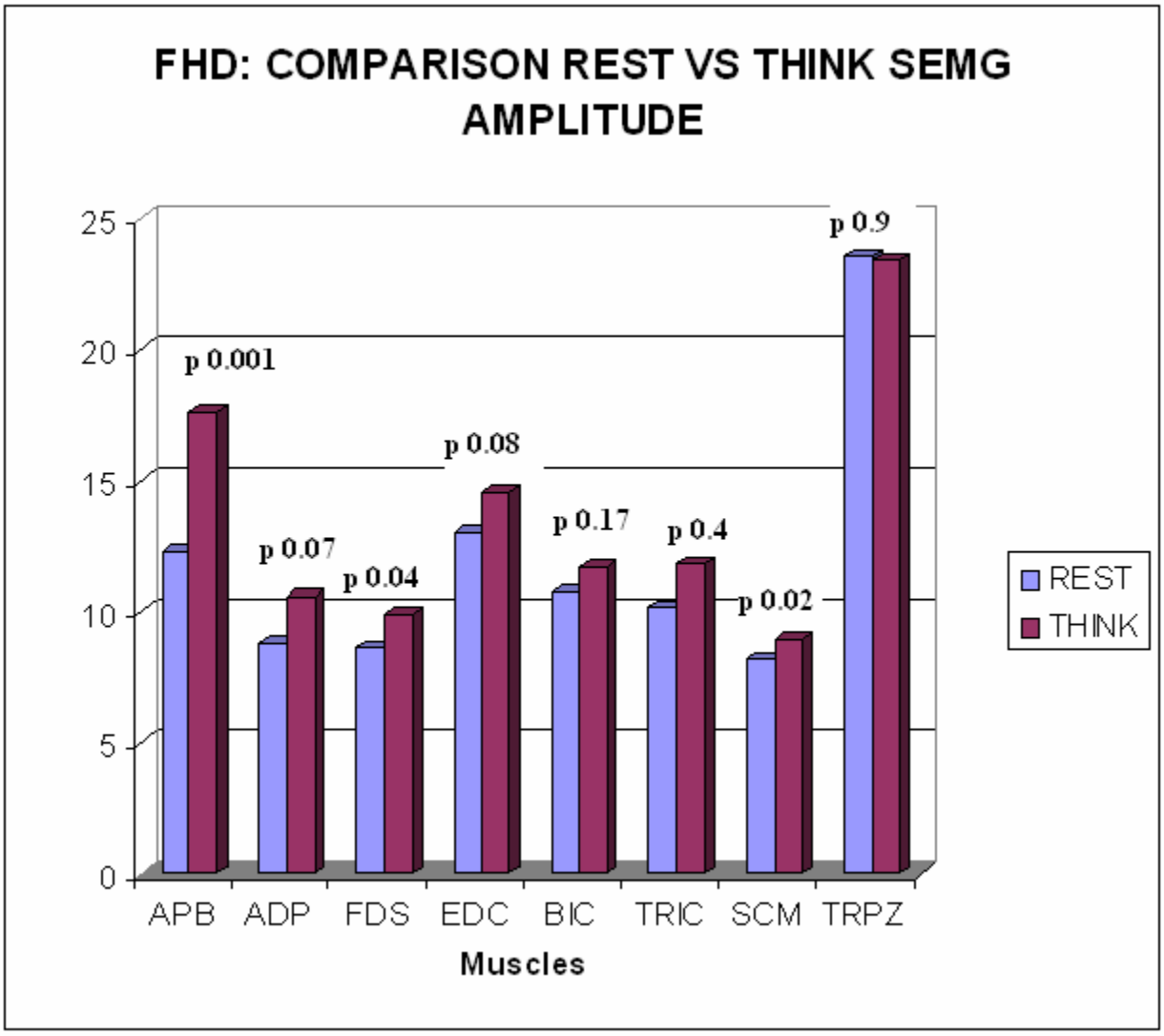
PHASE OF PREPARATION/ MOTOR IMAGERY

Table 4: comparison of SEMG amplitudes during preparation, thinking, motor imagery :

Muscle Mean (μV) SD	Normal	FHD	p value
APB	**12.72** 5.86	**17.62** 7.45	**0.04**
ADP	10.45 7.25	10.56 8.06	0.36
FDS	12.31 10.37	9.9 4.4	0.81
EDC	12.86 6.51	14.59 6.84	0.44
BIC	10.36 4.40	11.70 8.65	0.97
TRIC	13.92 5.97	11.84 7.76	0.12
SCM	10.64 5.42	8.95 2.50	0.22
TRPZ	22.69 13.19	23.39 17.16	0.97

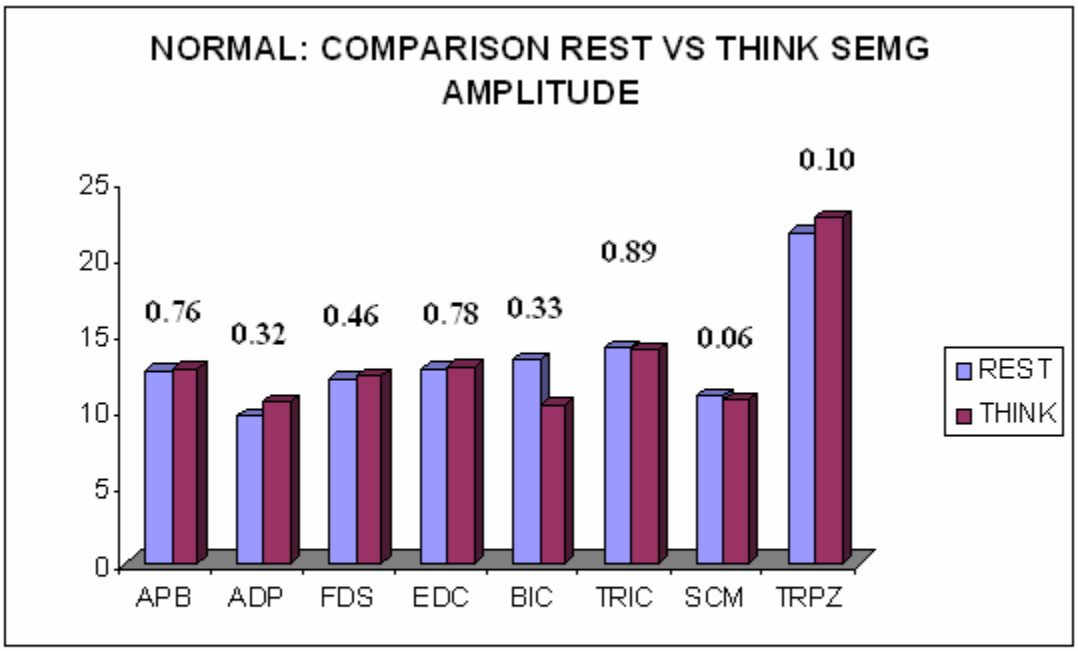
There was difference in the rectified mean SEMG between the two groups during this phase. This was prominent in the APB. Further analysis based on this observation revealed that there was an increase in the amplitude from resting baseline activity during this phase. This finding has also been highlighted in the graph plot earlier. Comparison between the rest and think SEMG show statistically significant differences in the APB, ADP and FDS groups of muscles as revealed in the bar chart below.

Figure 8: Bar chart showing the comparison of SEMG amplitude during rest and motor imagery in the FHD group. The 'p' values are indicated.



This phenomenon was identified by visual inspection of the individual EMG recordings in 12 subjects in the FHD group (12/ 20, 60%), **none of the normal controls showed a similar phenomenon** as shown in the figure below**.** These were observed mainly in the APB and EDC. The mean duration of such early activity was 32.4 seconds (SD 17.37 sec) before the onset of writing.

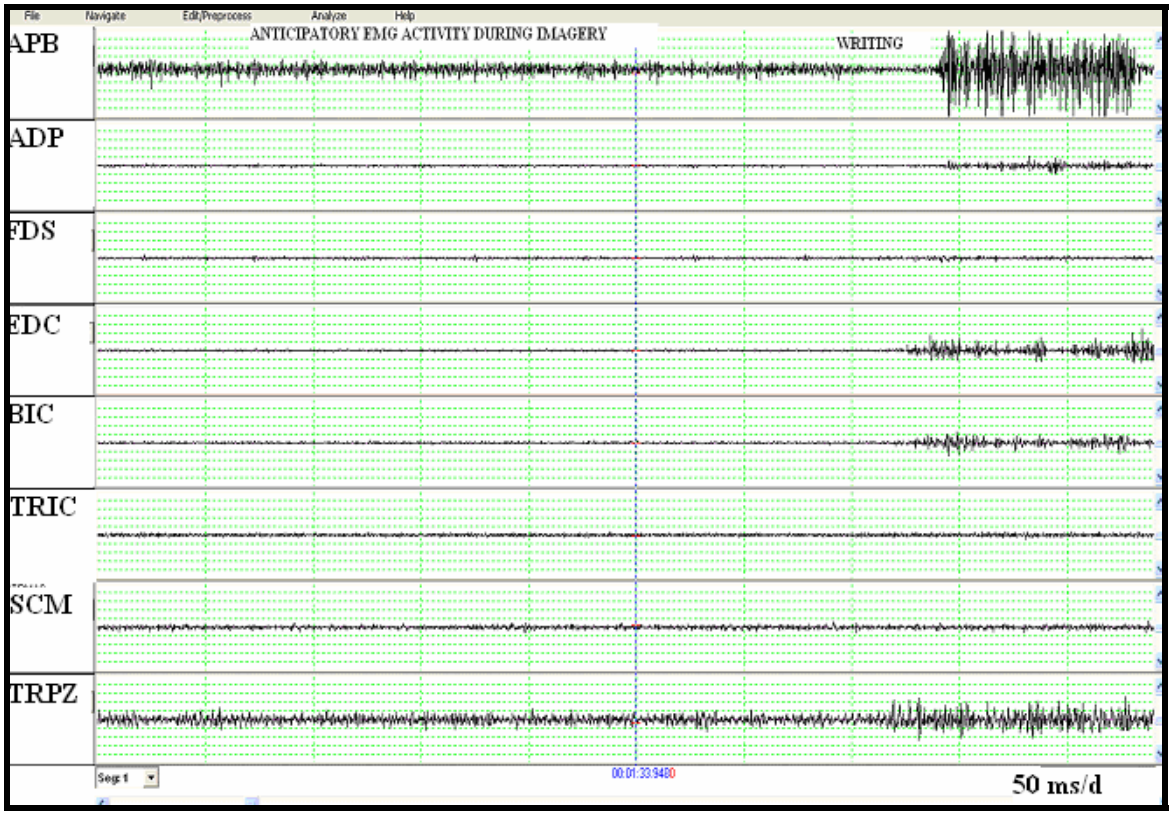
Figure 9: Bar chart comparing the SEMG amplitudes during rest and motor imagery in normal individuals. The 'p' values have been indicated.



FHD subjects with moderate/ severe dystonia (MF scale 3) were more likely to have anticipatory increase in activity compared to the milder forms. (OR 0.857, CI 0.41-1.7, p value 0.69). There was also no statistically significant correlation between duration of illness (> 2 years) and early activity. (OR 0.667, CI 0.35-1.27, p value 0.292).

An EMG recording from a FHD subject showing this phenomenon has been provided.

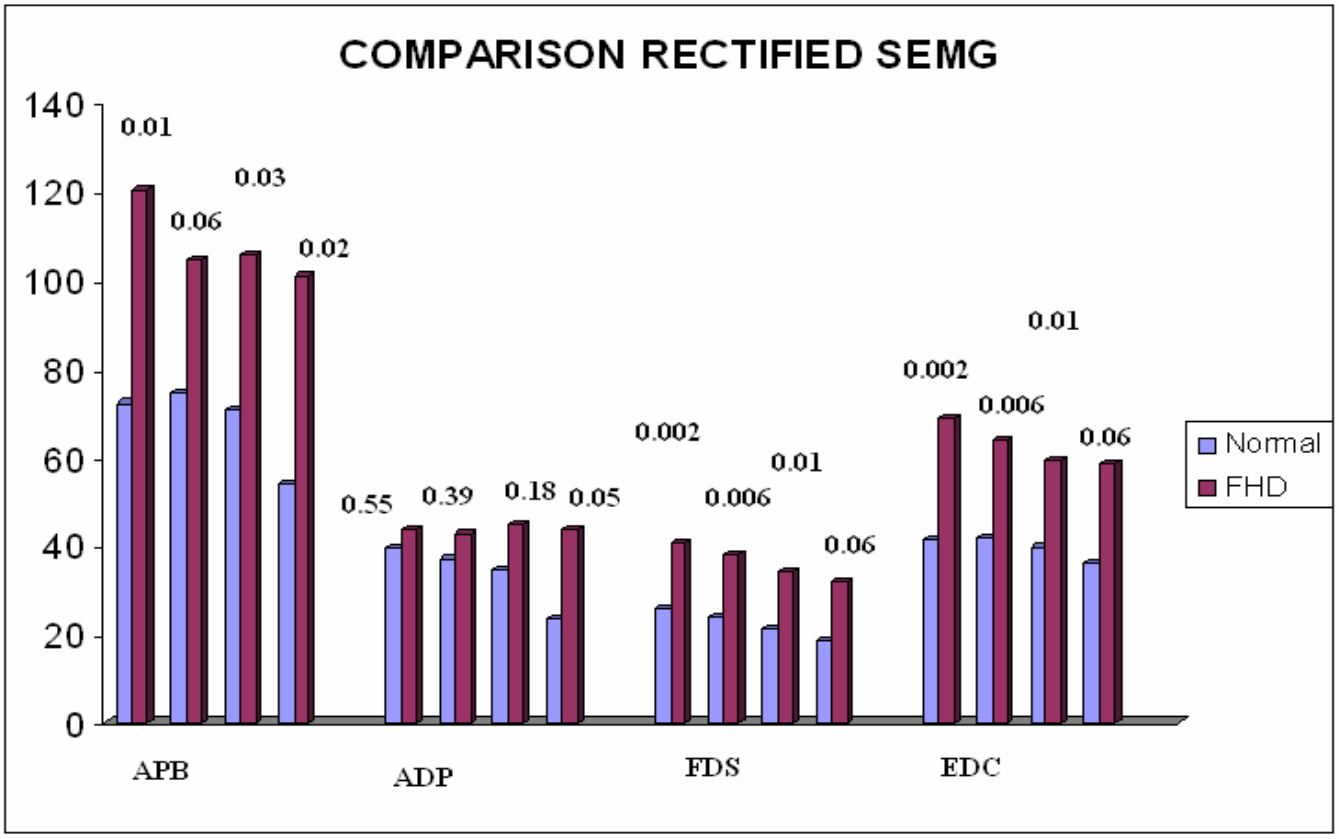
Figure 10: EMG recording showing increased activity in APB 36 seconds prior to onset of writing in a 46 year old subject with WC (Scale: 100 µV/div, 50 ms/div)



PHASE OF WRITING:

The mean SEMG amplitudes among the two groups were compared during the phase of actual writing. The control group usually completed the writing by 4 minutes and hence comparison between the two groups could be done only for the same duration.

Figure 11: Bar chart showing the mean rectified SEMG during the initial four minutes of writing between the FHD and control group with 'p' values to show statistically significant differences. ADP shows late increase in activity by 4 minutes.



Statistically significant differences were noted between the rectified mean SEMG amplitudes between the two groups. However the differences were confined to the following muscle groups: APB, FDS and EDC. ADP showed significant differences only towards the the 4th minute. The rest of the proximal and intermediate group of muscles did not show any significant differences. The mean values and standard deviation of each muscle throughout the entire duration of writing for the FHD group is as given in table 3.

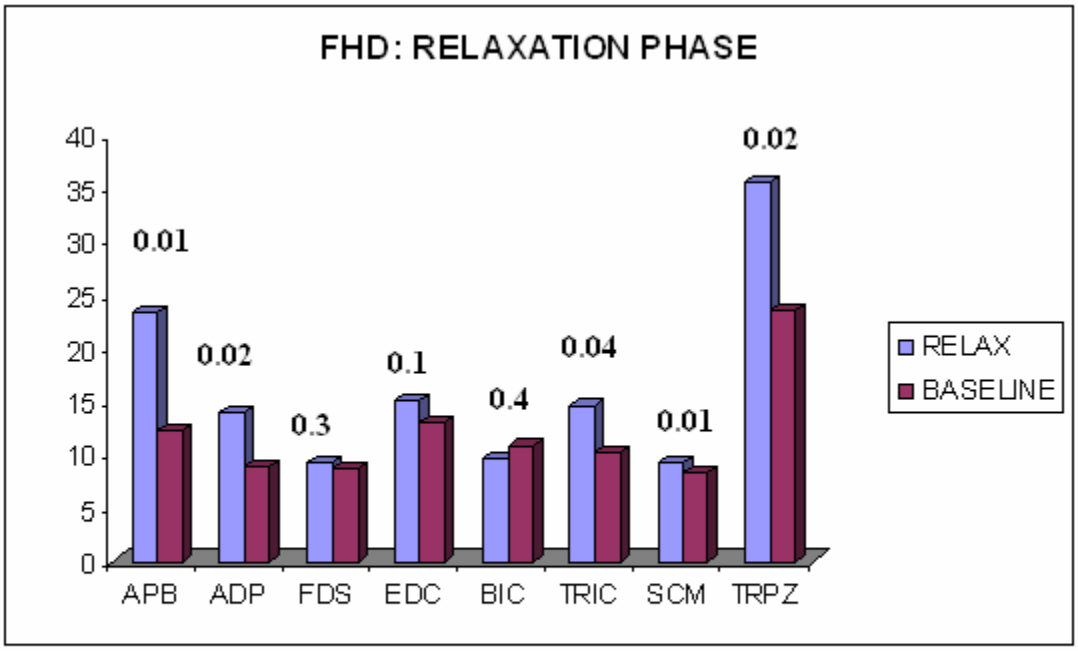
EMG AFTER STOPPING WRITING AND DURING RELAXING:

Table 5: Rectified mean SEMG during the phase of relaxation

Muscle Mean (SD)	Normal	FHD	p value
APB	12.83 (6.24)	23.28 (19.48)	0.06
ADP	12.88 (8.41)	13.91 (10.16)	0.82
FDS	8.59 (2.39)	9.23 (3.65)	0.58
EDC	10.53 (3.59)	15.04 (7.13)	**0.03**
BIC	10.58 (2.69)	9.58 (3.23)	0.34
TRIC	17.32 (6.15)	14.6 (10.33)	0.09
SCM	9.92 (1.58)	9.17 (2.36)	0.30
TRPZ	22.97 (13.90)	35.48 (24.02)	**0.04**

Careful interpretation of these values shows that the SEMG amplitudes during the phase of relaxation are significantly higher in the EDC and TRPZ in the FHD group. There is a trend towards significance in the APB and TRIC as well. The baseline resting values between the two groups were comparable as mentioned before. **A completely relaxed muscle is expected to show only baseline activity after stopping writing**. A comparison was made between the SEMG amplitude after stopping writing (during the relaxation phase) and baseline activity in both the groups. The FHD group showed statistically significant differences.

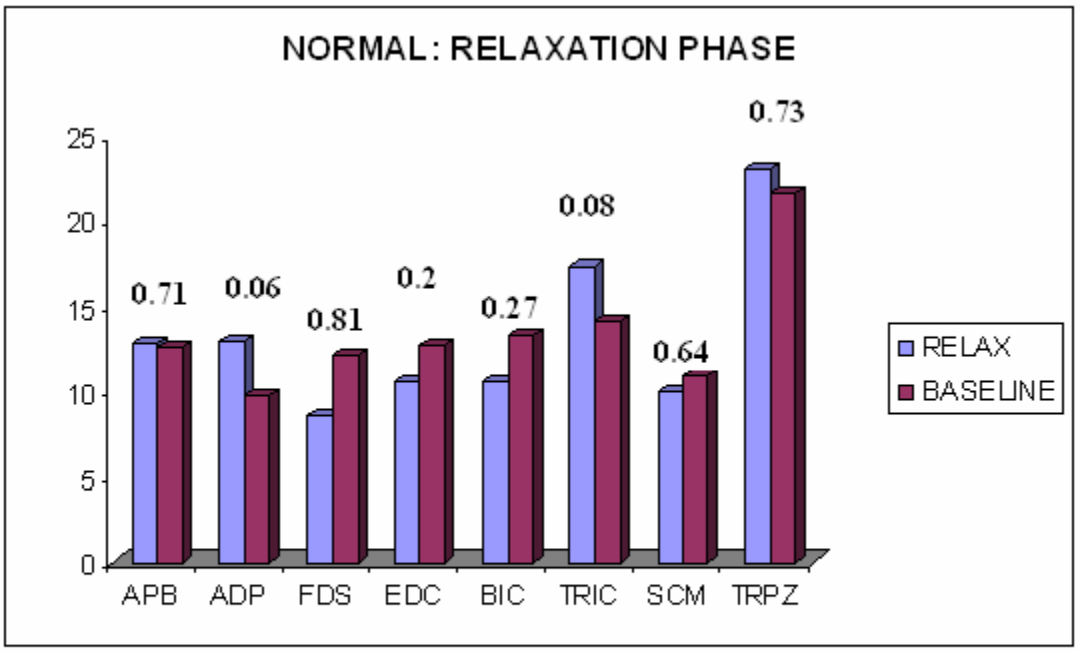
Figure 12: Bar chart comparing the SEMG amplitude after stopping writing with the baseline resting activity in the FHD group. The 'p' values are also indicated.



The bar chart clearly shows statistically significant differences in the APB, ADP, TRIC, SCM and TRPZ. The individual muscles in FHD take time to completely relax even after stopping writing. This phenomenon was not seen in the control group.

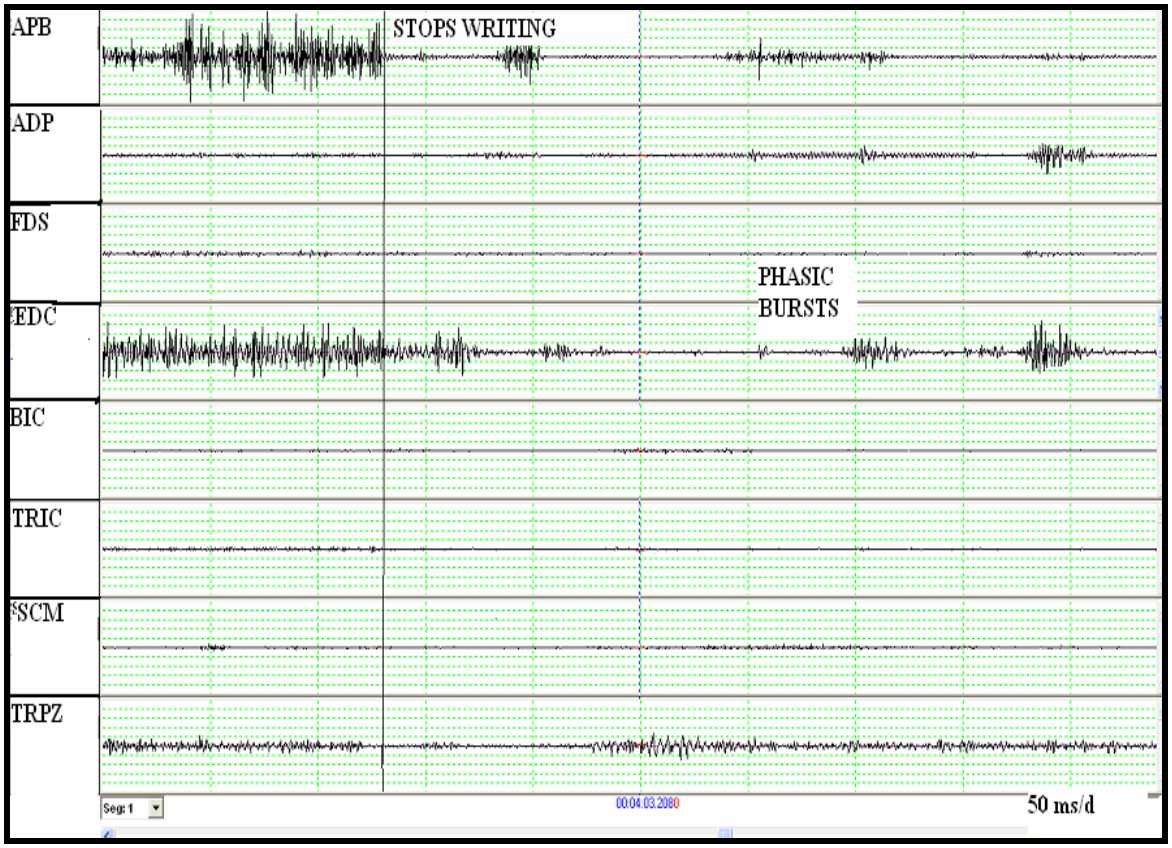
All the EMG recordings were meticulously inspected, such delayed relaxation was seen in 18 FHD subjects. The mean time for relaxation was 33 sec (SD 25.68 s). The delay in relaxation did not correlate with the severity of dystonia (for FM scale 3 dystonia, OR 0.86, CI 0.69-1.06, p 0.33). There was no correlation between the duration of illness and occurrence of this phenomenon. (OR 0.86, CI 0.71-1.05, p 0.39).

Figure 13: Bar chart showing the SEMG amplitudes during relaxation compared with the baseline activity. There is no statistical significance as indicated by the 'p' values.



The EMG recording of a FHD subject showing phasic bursts even after stopping writing has been provided below.

Figure 14: EMG recording from a 25 year old gentleman showing phasic bursts of activity in the EDC and APB even after stopping writing. (Scale: 150 µV/ div, 50 ms/div, for EDC 75 µV/div has been used to show the activity more clearly).



CO-CONTRACTION

Co-contraction of antagonistic muscle groups is the essential pathophysiological feature described in FHD. Co-contraction was identified by the presence of synchronized contraction/ bursts between agonist- antagonistic groups. EMG pattern of co-contraction was identified in all the FHD subjects. However, the number of agonist-antagonist groups showing co-contraction varied, the break-up is as given below. Most common type identified was repetitive rhythmic bursts of activity, noted in 16 subjects. Uniform co-contraction was identified in 4 subjects.

Figure 15: EMG recording showing phasic bursts of co-contraction involving APB-ADP, FDS-EDC, BIC-TRIC. (time scale: 200 ms/div)

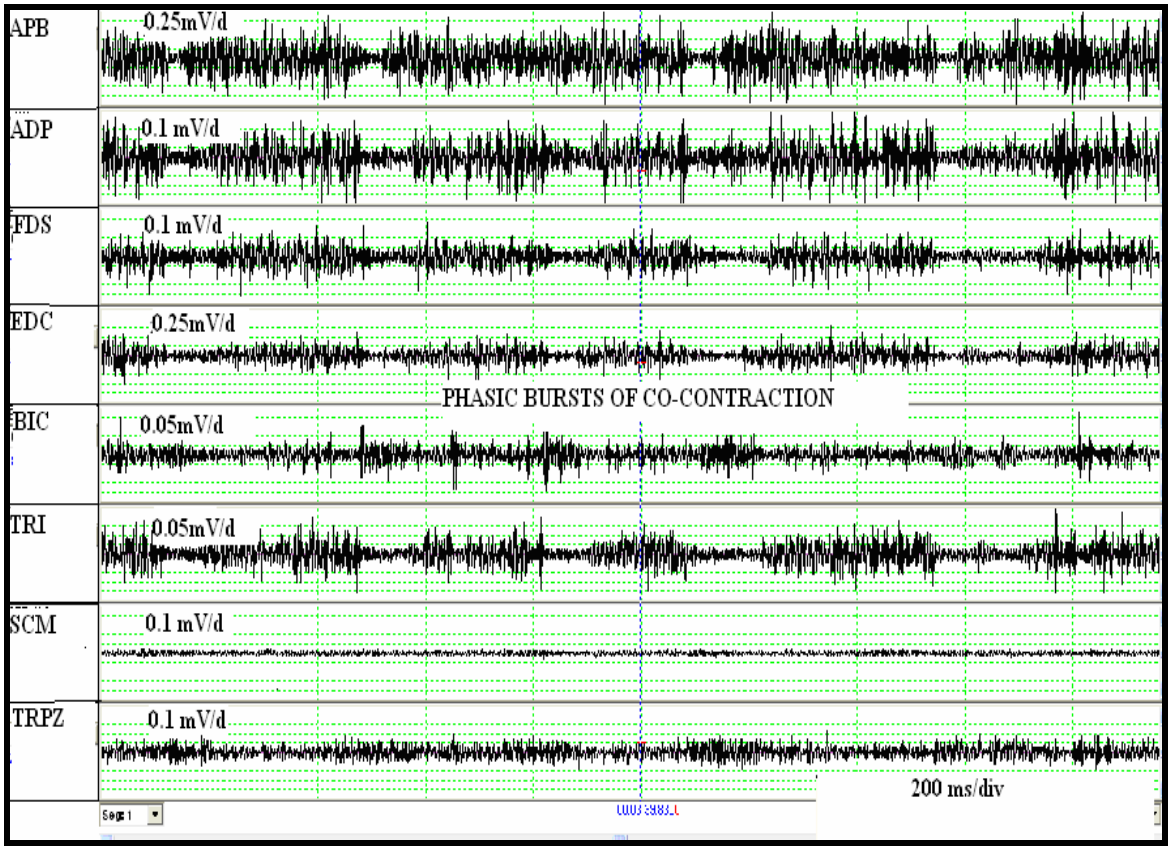


Figure 16: pattern of co-contraction among different antagonistic pairs

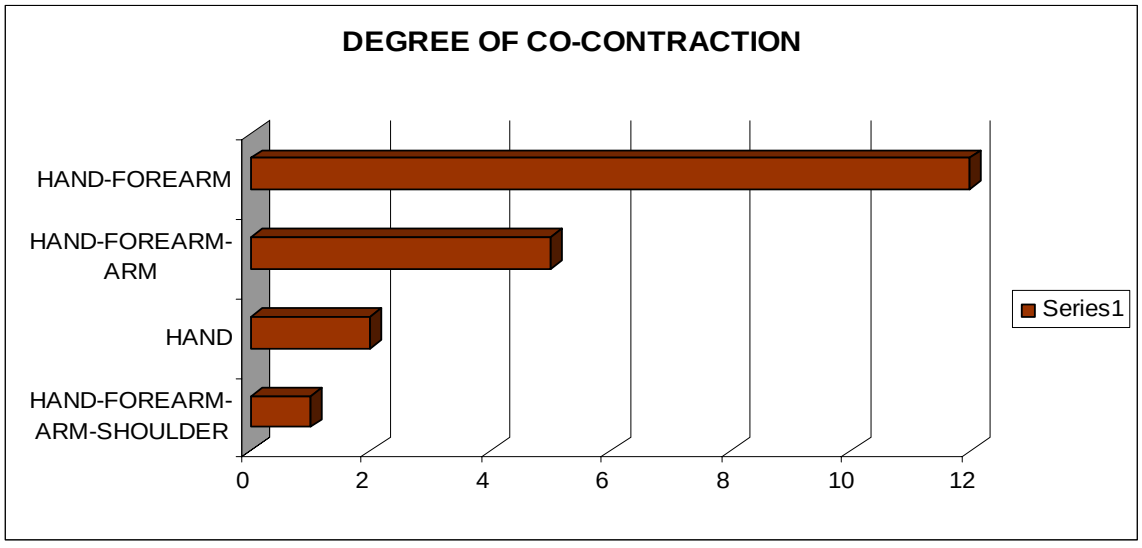
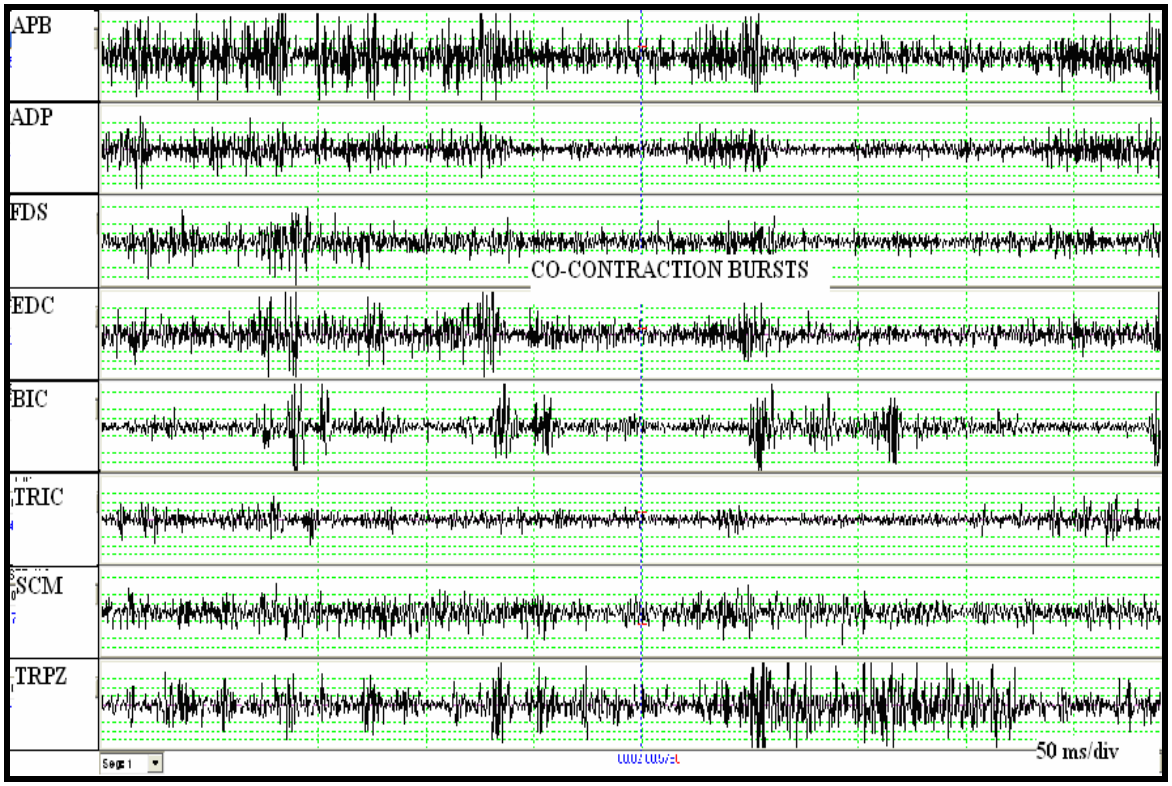


Figure 17: EMG recording from FHD subject showing co-contraction bursts involving all groups of muscle (scale: 50 µV/div, 50ms/div)



ONTOGENY OF MUSCLE RECRUITMENT

The SEMG recordings were meticulously reviewed to identify the order of muscle activation during the initiation of writing. The time latencies (in ms) to each muscle recruitment was noted and the observations are as given below

Controls:

APB was the first muscle to show activity in 12/ 16 subjects (75%). EDC and ADP showed activity first in 2 each. The least active muscle was Sternomastoid in 15 and trapezius in one. Early activation of trapezius before forearm muscles was seen in one subject.

FHD subjects:

APB was the first muscle in 14/ 20 subjects (70%). EDC was the first muscle in 4 and ADP/ FDS in one each. The last muscle to be activated was triceps in 13, sternomastoid in 6 and trapezius in one. Trapezius showed early activation in all but 2 subjects, recruitment was usually very early.

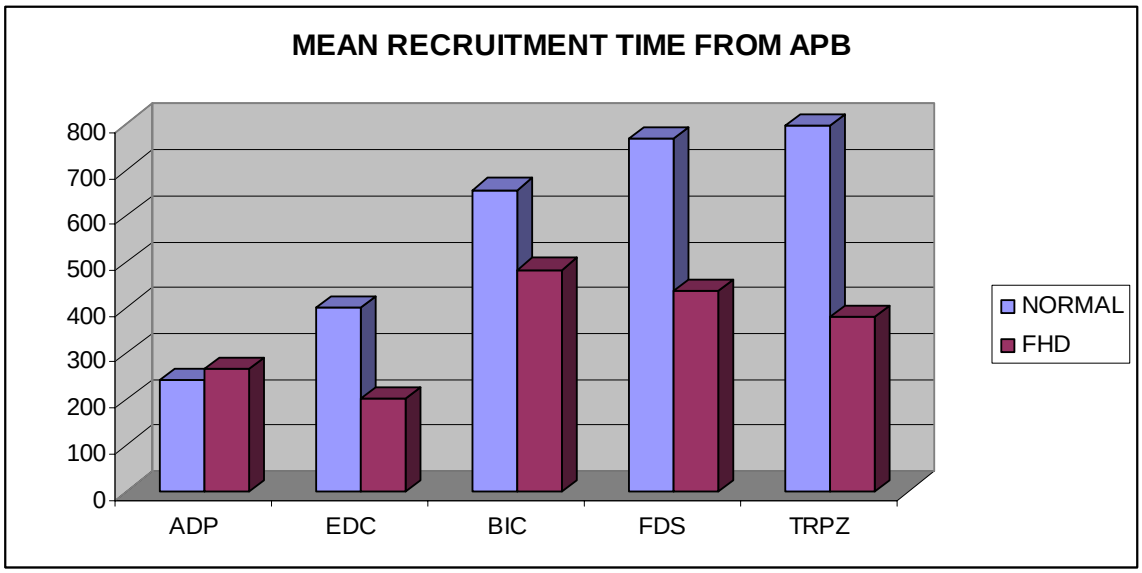
The recruitment times in milliseconds were taken with reference to APB activation. The distribution of mean and standard deviation is as follows. The FHD group has high standard deviation suggestive of high dispersion. This can also be explained by the fact that in six FHD subjects the other muscles were activated before the APB. In view of the fact that the data were non-parametric, Mann Whitney test was used for comparison of recruitment times between the two groups.

Table 6: Mean time to recruitment of muscles from APB in milliseconds

Muscle Mean ms (SD)	Normal	FHD	p value
ADP	243.33 (218.65)	265 (299.60)	0.49
FDS	770 (506.31)	435 (685.39)	**0.02**
EDC	400 (368.67)	200 (417.70)	0.06
BIC	540 (257.87)	483.33 (657.31)	0.16
TRIC	2400 (1284.07)	2566.67 (1399.58)	0.58
SCM	Not active in majority	1405.88 (1015.29)	-
TRPZ	842.85 (391.67)	380.5 (796.19)	**0.001**

Note that FDS, EDC, BIC, TRPZ and SCM show earlier recruitment in FHD, could be consistent with the finding of rapid overflow of motor activity. The differences in recruitment times were statistically significant for the FDS and TRPZ.

Figure 18: Bar chart showing recruitment times from APB in ms



The significance of the data may be limited by the high dispersion of values, however this again is reflective of the fact that the entire group is heterogenous and different patterns of activation are seen.

Two EMG recordings showing the pattern of activation in a control and FHD subject have been provided

Figure 19: Different pattern of activation of FHD and controls (SCM is not included in graph as activity seen late)

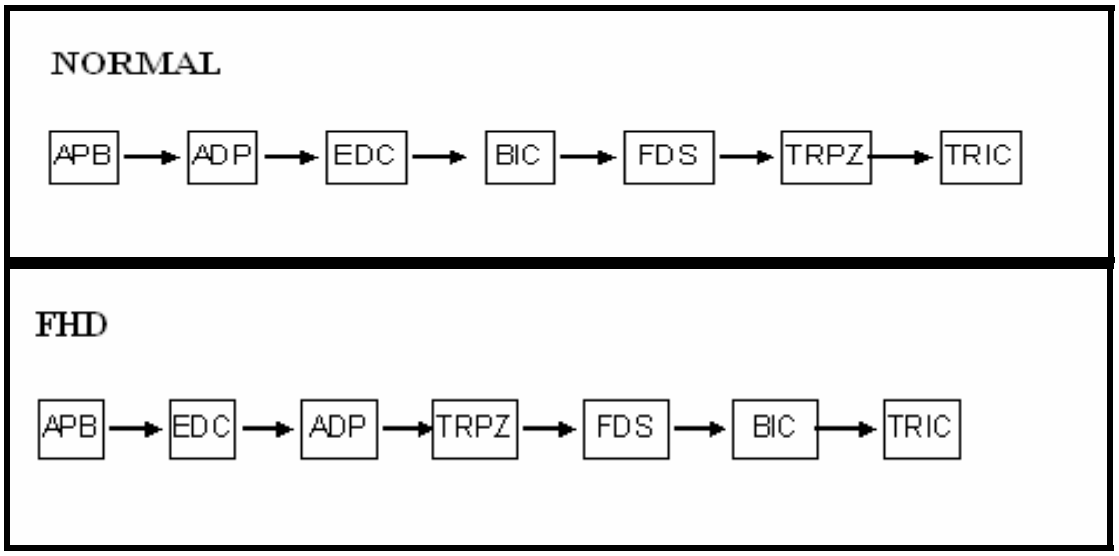


Figure 20: EMG recording with distal to proximal recruitment in normal

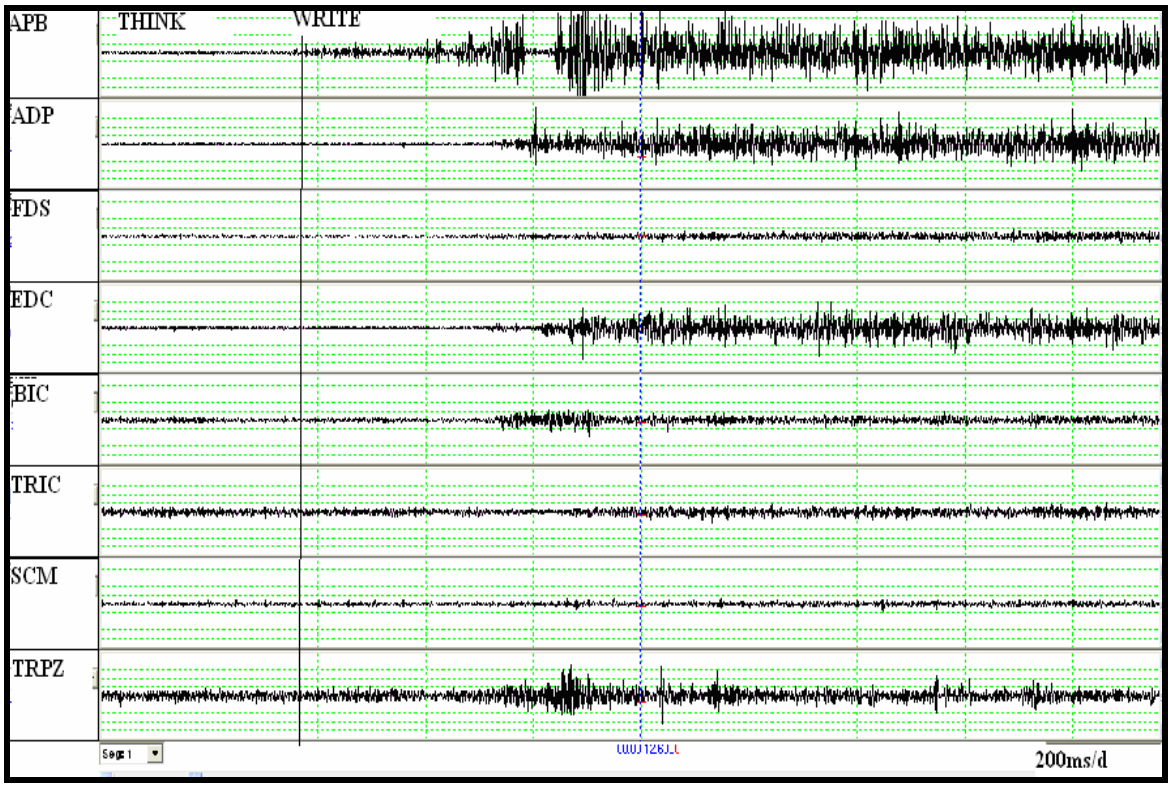
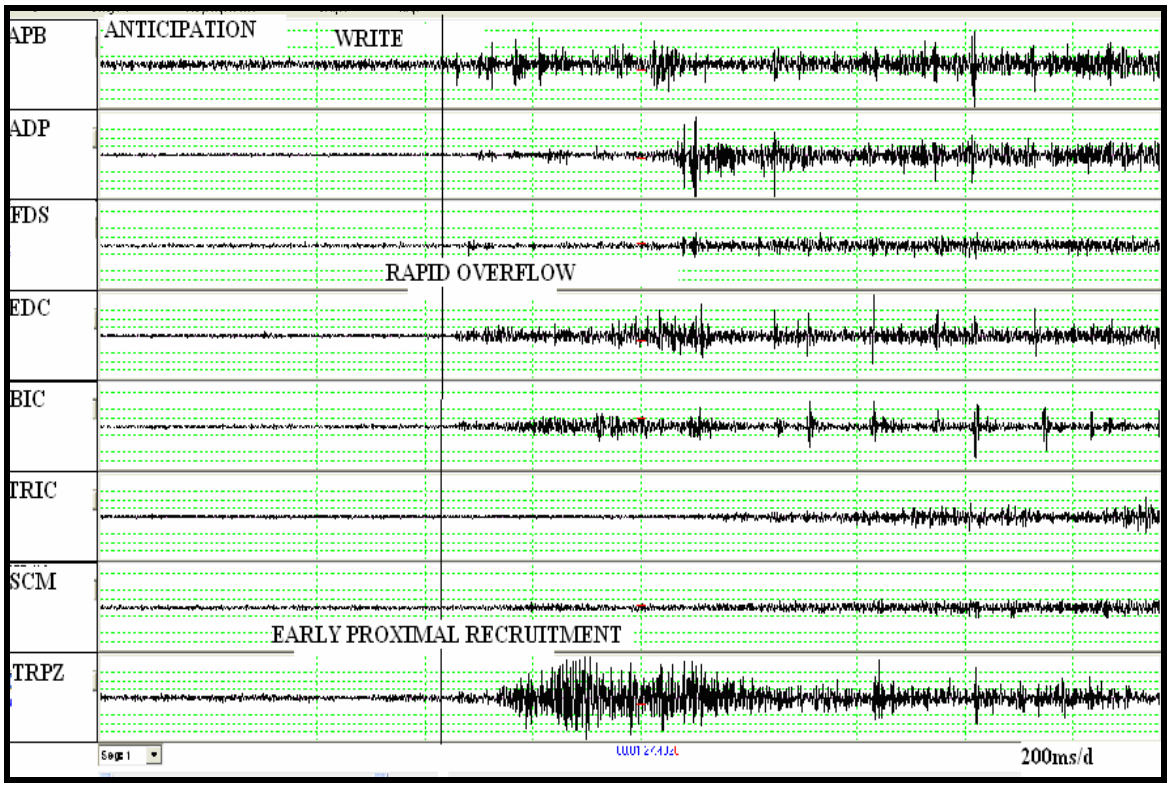


Figure 21: EMG recording in a FHD subject showing earlier proximal activity



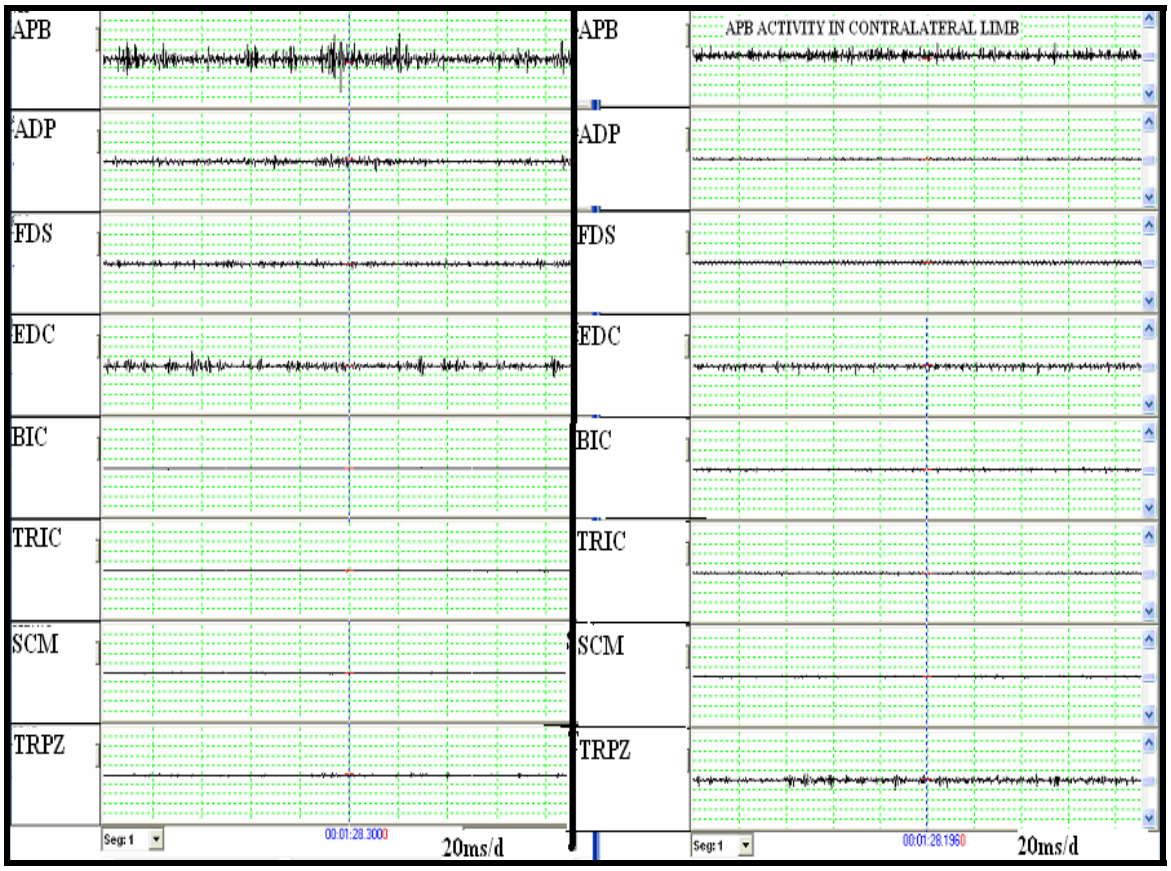
The next section will deal with EMG activity seen in the contralateral limb during writing. The contralateral limb activity will also be discussed in terms of rectified SEMG amplitudes, mean latencies and mirror movements.

CONTRALATERAL LIMB ACTIVITY

Coherent involuntary EMG activity in the muscles of the resting contralateral limb (left side) during the course of writing with the right upper limb was considered suggestive of mirror movement. EMG activity in the contralateral upper limb was noted in all FHD subjects (100%). Similar patterns were noted in 8 normals (50%). Mirror movements were noted commonly in the EDC, APB and trapezius group of muscles. This was commonly in the form of increased activity (though of lower amplitude) during writing in

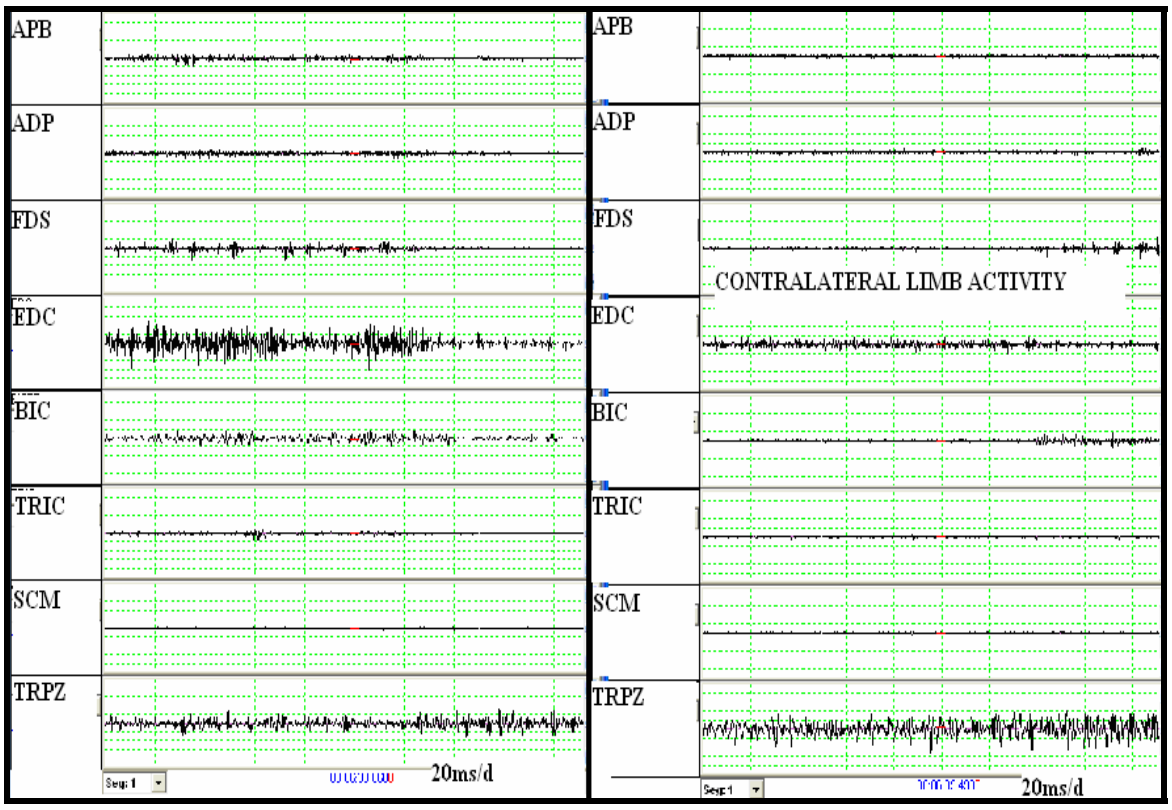
the contralateral limb muscles. FHD subjects were more likely to have contralateral limb activity. (OR 2, CI 1.225 – 3.265, p value 0.002).

Figure 22: EMG recording from FHD subject showing contralateral APB activity.



In the above recording, the gain has been changed in the left upper limb for better visualization of the EMG activity. (scale: 500 µV/div, 250 µV/div, 20 ms/div).

Figure 23: EMG recording from 45 year old FHD subject showing contralateral EDC, FDS, BIC and TRPZ activity. (scale: 250 µV/div, 100 µV/div, 20 ms/div)



RECTIFIED MEAN AMPLITUDE FROM THE CONTRALATERAL LIMB

Surface EMG recordings were obtained, the data was filtered and integrated. The rectified mean amplitude from the left upper limb muscles is as given in the tables below. The plot showing the distribution of the recording over the time frames is also provided.

Table 7: Control: Rectified SEMG from the contralateral limb during the writing task

		APB	ADP	FDS	EDC	BIC	TRIC	SCM	TRP
REST	**MEAN**	14.88	11.53	12.62	9.06	10.16	13.47	10.91	15.14
	SD	8.60	8.54	7.56	3.82	4.09	6.15	3.98	11.68
THINK	**MEAN**	14.55	11.02	12.25	9.25	10.80	13.75	10.77	16.46
	SD	8.23	6.15	6.76	4.08	3.50	6.13	4.04	12.22
1 MIN	**MEAN**	14.26	11.61	13.08	11.41	11.3	14.00	11.33	17.95
	SD	9.24	8.24	7.64	6.95	4.79	9.97	4.32	12.00
2 MIN	**MEAN**	15.03	10.71	13.45	12.03	11.16	14.36	11.03	18.65
	SD	9.43	6.07	8.09	7.71	4.50	9.84	4.17	11.97
3 MIN	**MEAN**	15.05	10.53	13.39	11.06	11.42	15.10	11.18	18.80
	SD	9.16	5.57	8.52	6.23	4.80	8.63	4.16	11.33
4 MIN	**MEAN**	13.4	11.66	11.34	8.44	10.38	10.28	9.24	17.85
	SD	1.79	6.12	3.81	2.88	2.15	1.99	2.38	6.79
RELAX	**MEAN**	13.62	9.86	11.33	10.02	9.66	13.43	9.78	15.16
	SD	5.61	4.66	4.22	3.73	3.02	5.82	3.41	8.11

Figure 24: Graph showing SEMG left UL over different time frames in controls

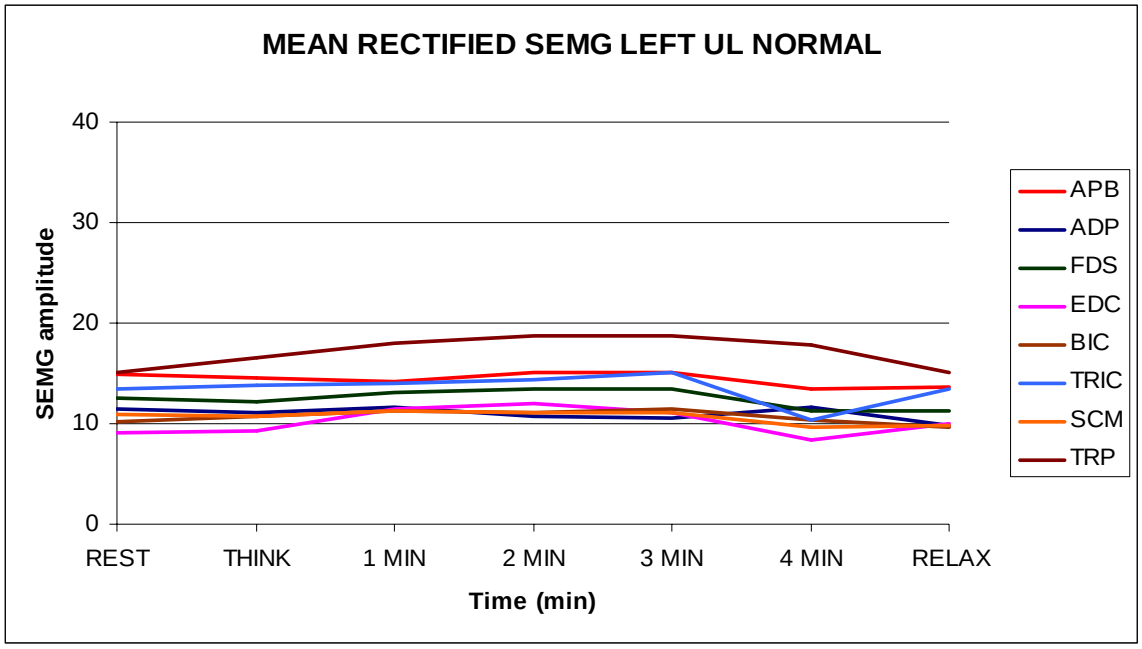
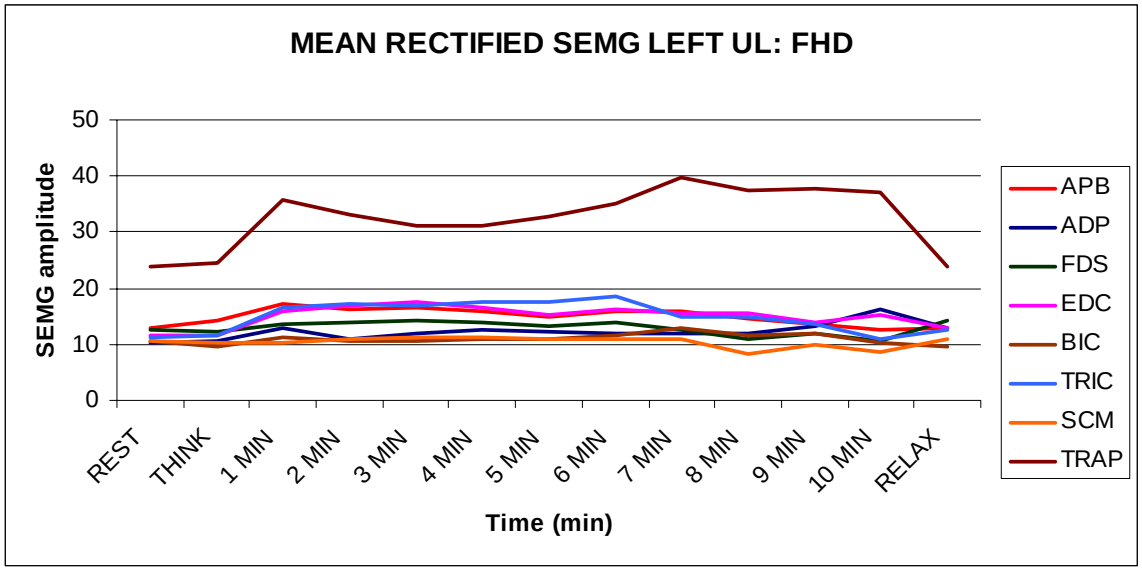


Table 8: Mean Rectified SEMG from the left upper limb of FHD subjects

		APB	ADP	FDS	EDC	BIC	TRIC	SCM	TRP
REST	**MEAN**	12.92	10.13	12.46	11.49	10.65	11.34	10.47	23.86
	SD	4.15	7.61	5.63	5.39	6.34	4.65	5.89	18.14
THINK	**MEAN**	14.10	10.45	12.29	11.685	9.53	11.69	10.30	24.53
	SD	5.34	7.78	5.47	5.81	2.82	4.94	5.52	16.90
1 MINUTE	**MEAN**	17.33	13.05	13.72	15.98	11.26	16.59	10.40	35.69
	SD	9.59	10.16	7.20	5.71	3.86	12.48	4.31	19.44
2 MINUTE	**MEAN**	16.36	10.79	13.83	17.05	10.65	17.13	11.05	32.97
	SD	9.30	4.19	6.77	6.94	4.07	12.02	4.59	15.92
3 MINUTE	**MEAN**	16.54	11.85	14.21	17.61	10.56	16.92	11.33	31.07
	SD	8.93	5.88	7.45	7.96	3.67	9.87	4.85	14.48
4 MINUTE	**MEAN**	15.79	12.6	13.95	16.61	11.05	17.47	11.23	31.14
	SD	7.44	7.60	7.06	7.78	5.03	10.27	4.82	15.62
5 MINUTE	**MEAN**	14.77	12.37	13.38	15.28	10.861	17.42	10.86	32.75
	SD	5.89	9.83	6.40	6.12	5.17	11.09	5.27	17.56
6 MINUTE	**MEAN**	16	11.96	13.83	16.31	11.67	18.70	11.03	35.25
	SD	5.97	6.91	6.06	6.74	4.58	12.44	5.84	16.81
7 MINUTE	**MEAN**	15.84	11.99	12.52	15.56	12.98	15.04	11.05	39.64
	SD	4.89	7.22	4.59	8.45	9.84	8.27	7.64	19.36
8 MINUTE	**MEAN**	14.5	11.86	10.97	15.44	11.48	14.75	8.41	37.35
	SD	6.85	8.32	3.54	7.43	4.38	8.32	2.61	17.46
9 MINUTE	**MEAN**	13.62	13.27	12.03	13.92	11.9	13.52	9.88	37.90
	SD	5.40	12.42	5.16	5.86	8.47	7.03	4.81	16.33
10 MINUTE	**MEAN**	12.48	16.17	10.46	15.12	10.28	10.88	8.77	37.02
	SD	4.47	15.48	2.80	8.18	5.85	5.30	1.52	15.15
RELAX	**MEAN**	12.81	12.84	14.29	12.98	9.49	12.57	10.79	23.87
	SD	5.077	10.85	9.86	7.82	3.85	6.84	6.33	19.05

Figure 25: Graph showing mean rectified SEMG in the contralateral limb in FHD group.



COMPARISON OF RECTIFIED MEANS OF CONTROL WITH FHD GROUP

The unpaired t – test was used to compare the rectified means between the two groups. For non-parametric data, Mann Whitney test was used. The relevant results are given in the table below. These data provide further evidence to support the fact that the non-writing hand also shows activity in FHD subjects compared to normals. This could be as a result of "contralateral motor overflow" or "mirror dystonia". The activity is more marked in the trapezius and EDC group of muscles. The question whether this can be termed to be "pre-dystonia" can be answered only on serial followup of these subjects.

Table 9: comparison between the rectified mean SEMG of control and FHD subjects. We are interested in the the 'p' value and the 95% confidence interval.

	REST	THINK	1 MIN	2 MIN	3 MIN	4 MIN	RELAX
APB	0.92	0.51	0.08	0.47	0.45	0.13	0.75
ADP	0.30	0.44	0.49	0.35	0.32	0.56	0.86
FDS	0.85	0.84	0.81	0.87	0.76	0.52	0.71
EDC	0.12	0.15	**0.02**	0.03	**0.01**	**0.01**	0.51
BIC	0.79	0.24	0.98	0.72	0.55	0.62	0.46
TRC	0.34	0.32	0.22	0.25	0.56	0.10	0.27
SCM	0.80	0.77	0.52	0.99	0.92	0.46	0.61
TRP	0.10	0.04	**0.001**	**0.001**	**0.002**	**0.03**	0.07

As mentioned before, there was EMG activity from the contralateral left upper limb during writing in all the subjects and eight normals. Of the normals, TRPZ showed activity in all eight. EMG activity was obtained from the TRPZ alone in three normals. Concomitant ADP, EDC, BIC activity was seen in 4, FDS activity in 3, APB in 2 and SCM/ TRIC in one each.

The mean latency to activity in the contralateral limb after initiation of writing was noted. The values are as mentioned in the next table.

Table 10: Mean duration of recruitment of muscles in the contralateral limb (latency calculated from right APB activity)

	Mean (ms)	SD
TRAP	1456.25	1090.52
SCM	2080	704.98
TRIC	2680	1283.91
BIC	1746.67	1162.03
EDC	1960	958.85
FDS	2192.85	1200.8
ADP	2583.33	931.98
APB	3054.54	1114.75

There appears to be a proximal – intermediate – distal spread of activity in the contralateral limb. This pattern was seen in 14/20 FHD subjects (70%). This pattern is most likely due to the contralateral overflow of activity.

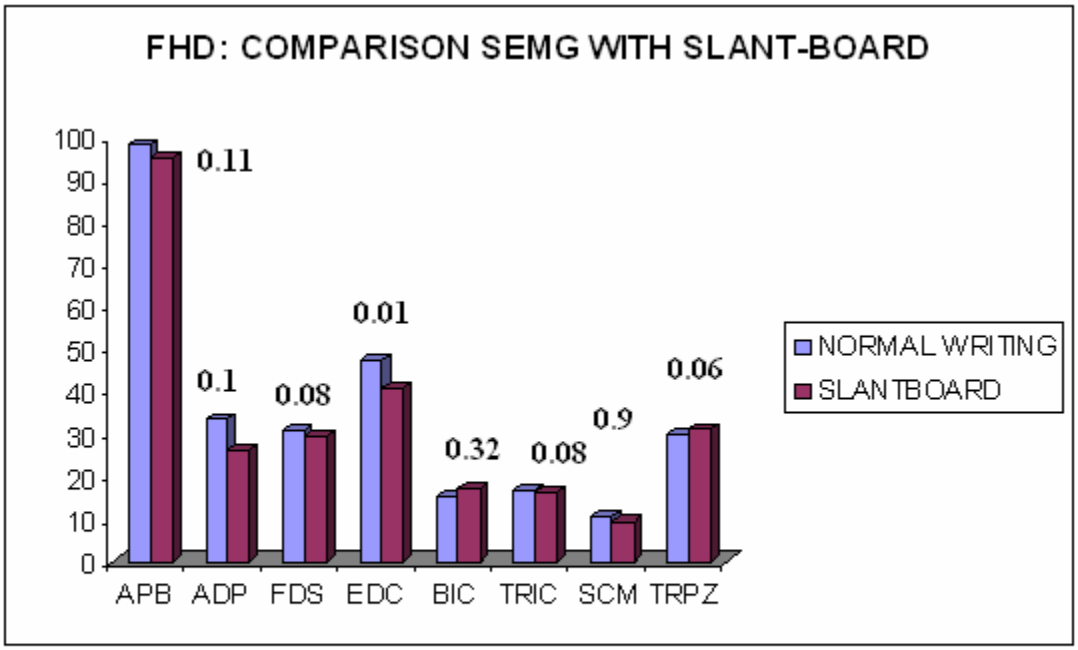
WRITING ON SLANT BOARD

It is a common observation that FHD patients report that they are able to write much easier on a black board. Six FHD subjects in the study group were asked to also write the paragraph on a slant board with a usual ball point pen. The SEMG recording was done and the rectified mean SEMG was compared between the two groups using paired t-test.: The SEMG amplitude was lower in the distal and intermediate group of muscles, (EDC significant difference) proximal group appeared more activated during slant board writing. The quality of script was similar in both the groups. Mean time to completion was more while writing on the slant board (499 seconds compared to 430 seconds).

Table 11: Comparison of mean SEMG amplitude (μV) between normal writing and writing on a slant board in FHD

Mean (SD)	**WRITING BOARD**	**SLANT BOARD**	**SIGNIFICANCE**
APB	98.24 (49.65)	94.94 (49.65)	0.11
ADP	33.46 (18.07)	26.52 (16.18)	0.10
FDS	30.82 (15.83)	29.32 (14.88)	0.08
EDC	47.14 (26.44)	40.74 (18.4)	0.01
BIC	15.48 (3.08)	17.5 (5.32)	0.32
TRIC	16.82 (7.52)	16.44 (8.53)	0.08
SCM	10.38 (1.06)	9.5 (0.58)	0.9
TRP	29.90 (6.42)	31.16 (16.95)	0.06

Figure 26: comparison of SMG amplitudes



There was a trend towards more proximal muscle involvement and lesser distal involvement as expected. However a larger sample will be needed to validate these findings.

ASSESSMENT OF FUNCTIONAL DISABILITY

As stated earlier, the functional disability of the subject eventually reflects on the speed of writing and the legibility of the script. Using a composite end point including both the impaired speed (> 7 minutes) and illegible script (legibility scores 1,2), statistical analysis was done using both Chi square and subsequently logistic regression analysis to check if any of the baseline characteristics or analyzed SEMG parameters had statistically significant correlation with functional disability. Only FM scale correlated with functional disability.

Table 12: association of baseline and SEMG parameters with functional disability

parameter	Odds ratio	Confidence interval	P value
Treatment naive	1.33	0.41 – 4.31	0.606
Illness duration > 2 years	0.92	0.53 – 1.56	0.766
Age > 40 years	3.33	0.55 – 19.94	0.06
Fahn Marsden score 3	**26**	**1.83 – 367.69**	**0.001**
SEMG amp > 80 μv	1.667	0.54 – 5.168	0.292
Anticipation	1	0.44 – 2.28	1.0
Delayed relaxation	0.867	0.71 – 1.06	0.389

FREQUENCY SPECTRAL ANALYSIS

Changes in spectral analysis in EMG can be used to identify muscles which are active during activity, could be used as a tool in the study of localized muscle fatigue.

Figure 27: An example of power frequency spectrum of right APB in a FHD subject during initiation of writing (mean 118.3 Hz) and end of writing (mean 99.8 Hz).

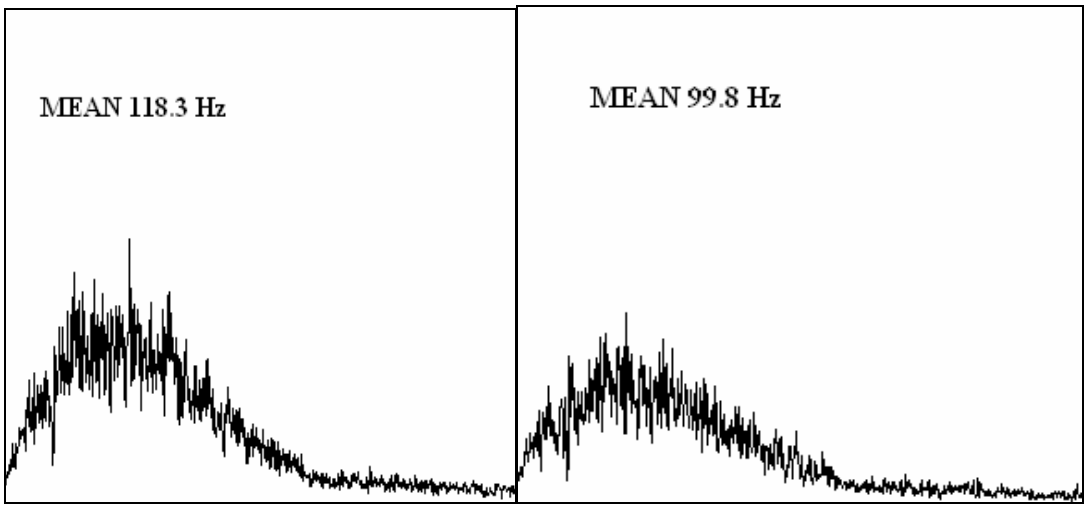
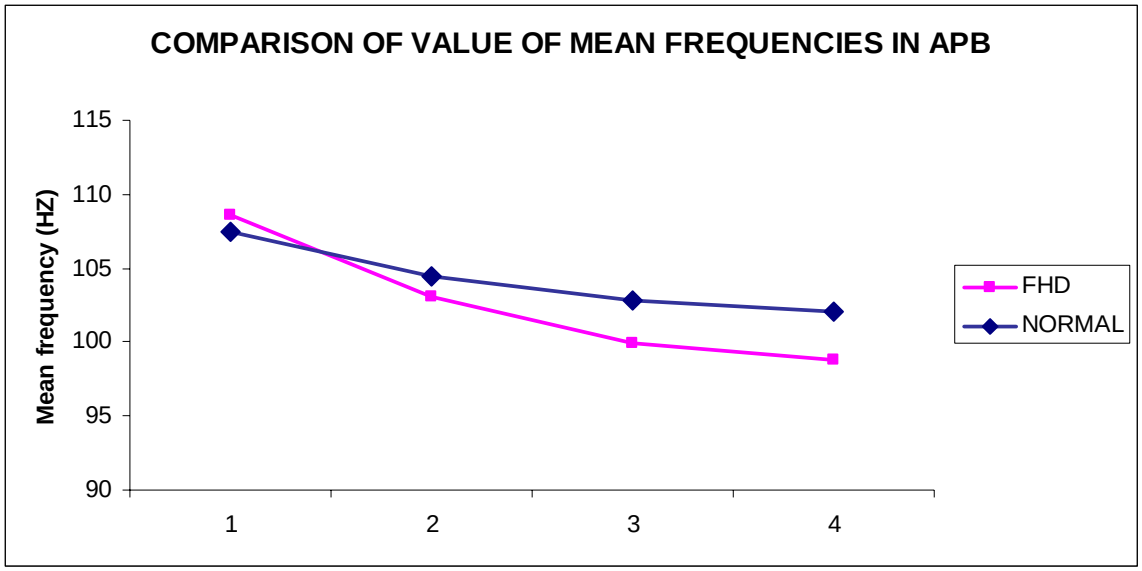


Figure 28: sample plot showing comparison of mean frequencies during different phases of writing between FHD subjects and controls



The plots indicate that there is a higher decrement in the mean frequencies during writing in the FHD group, the decrement also tends to occur earlier as shown by the early steep decrement. These could be indicator of early fatigue. The difference in slopes was however, not significant (independent t test, p values 0.66, 0.22, 0.24). The changes in the other muscles are as given in the tables below.

Table 13: Mean (SD) values of the mean frequency of the eight muscles (right side) in the power spectrum during different phases of writing in Normal controls. The percentage decrement in mean frequency values has also been indicated wherever applicable

		PHASE 1	PHASE 2	PHASE 3	PHASE 4	% decrement
APB	**MEAN**	107.57	104.4	102.8	102.0	5%
	SD	27.4	28.2	26.3	26.1	
ADP	**MEAN**	60.7	62.2	57.1	58.1	4%
	SD	33.9	32.3	32.4	36.8	
FDS	**MEAN**	90.6	95.1	100.8	110.9	
	SD	29.2	26.6	26.9	29.1	
EDC	**MEAN**	103.4	103.1	103.2	101.5	2%
	SD	18.9	15.6	15.2	12.7	
BIC	**MEAN**	77.3	77.3	77.5	74.4	4%
	SD	12.6	12.3	17.3	14.0	
TRIC	**MEAN**	43.9	43.4	40.7	41.4	5.6%
	SD	45.4	44.9	42.3	42.8	
SCM	**MEAN**	55.4	55.7	52.5	54.0	2.5%
	SD	51.7	49.9	47.1	47.6	
TRPZ	**MEAN**	57.7	60.3	59.6	58.3	
	SD	49.5	55.4	56.5	54.6	

Table 14: Mean (SD) values of the mean frequency of the eight muscles (right side) in the power spectrum during different phases of writing in FHD subjects. The percentage decrement in mean frequency values has also been indicated wherever applicable

		PHASE 1	PHASE 2	PHASE 3	PHASE 4	% Decrement
APB	MEAN	108.6	103.0	99.9	98.8	9%
	SD	29.8	29.7	30.4	29.8	
ADP	MEAN	87.0	83.8	82.7	83.1	5%
	SD	52.9	51.6	52.4	53.9	
FDS	MEAN	101.7	98.4	100.3	102.4	
	SD	31.1	30.5	30.6	30.1	
EDC	MEAN	109.0	111.1	111.3	111.4	
	SD	19.1	13.7	13.7	14.1	
BIC	MEAN	78.0	78.4	75.9	74.1	6%
	SD	31.6	31.1	29.7	31.1	
TRIC	MEAN	63.7	57.1	59.3	55.8	12%
	SD	57.4	47.3	51.2	48.6	
SCM	MEAN	67.3	64.22	58.4	58.1	14%
	SD	61.1	58.	55.9	56.6	
TRPZ	MEAN	55.2	53.1	52.6	55.3	
	SD	40.2	44.3	42.8	45.7	

The implications of these findings will also be discussed in the subsequent section.

DISCUSSION

The current focus on pathophysiology of Writer's cramp has been on the aspects of impaired surround inhibition, abnormal plasticity and the abnormal sensorimotor integration using mainly TMS and functional neuroimaging and their implications. However, there is scarce data on the objective description of the clinical phenomenology and temporo-spatial spread of activity. Surface EMG is a simple non-invasive test to provide a qualitative and quantitative assessment of this fascinating disorder.

The study proposed to identify the EMG patterns from WC subjects and compare them with healthy individuals. A novel 16 channel surface EMG recording was done using surface electrodes for 4 pairs of muscles in each upper limb. The use of customized software, multichannel (16) EMG including the contralateral normal limb also and objective assessment during performance of a specific "writing task" with different time frames (rest, preparing to write/ motor imagery, write and relax) were the most striking aspects of the methodology of this study which intended to provide further insight into possible neurophysiological abnormalities in this disabling disorder. Rectified mean SEMG, time latency to onset of muscle firing/ activation and spectral analysis were used to quantify the data. The concept of "functional disability" in terms of legibility and speed and its correlation with the EMG parameters and baseline demographics is also a novel way which will help in assessing the response to therapies. The study had some interesting observations as mentioned below.

The time taken to completion of writing was significantly higher in the FHD group and also correlated with disease severity. The most likely explanation for the same will be due to a motor execution problem secondary to abnormal cortical – basal ganglia circuits, the possibility of slowing as an adaptive phenomenon to enhance movement accuracy seems less likely. The EMG correlates contributing to slowing include co-contraction and abnormal agonist bursts.

The muscles involved, degree and pattern of involvement during writing showed variations especially in the WC group. These findings reflect the heterogenous spectrum of this focal disease.

The mean rectified EMG was compared between the two groups. There was a statistically significant difference in the mean amplitudes between the two groups during the different time frames of the task. The main muscles implicated include the APB, EDC and FDS. Identification of higher activity among the muscle groups can help in refining the use of botulinum toxin and biofeedback techniques for choosing proper target muscles.

Increase from the baseline activity during the 'preparatory' phase/ stage of 'motor imagery' is an important observation. This has been depicted in the plot, bar chart (figure 7, 8) as well as the table (4). One such recording from a WC subject has also been provided. The mean amplitude of APB, ADP, FDS and EDC showed significant difference during motor imagery compared with baseline. The mean duration of such "early onset" activity was 32.4 seconds before the actual initiation of writing. This

finding has important implications. The early pre-task activity can be attributed to "anticipation" and "prelearned behaviour" increasing the central motor drive. Similar descriptions have been made by Quartarone et al [52] using MEPs and Murase et al [51] who noted impaired modulation of premovement sensory input with loss of normal attenuation of the SEPs during the preparatory phase. Nowak et al using the precision hand grip model demonstrated shorter latency responses and grip force overshoots during the initial tasks which subsequently adapted to normal steady state values. [50] The question regarding the effect of this early anticipatory activity: whether just an incidental finding or it per se leads to higher SEMG amplitudes and worsening disability needs to be addressed. In our analysis, we found that though such a phenomenon was seen exclusively in the WC group, it did not contribute significantly to the functional disability. This phenomenon also should be amenable to biofeedback and proper relaxation techniques may make a difference to overall treatment of the patient.

The graph depicting the rectified SEMG amplitudes during the different stages of the writing task shows some striking differences as already mentioned.

- "anticipatory" increase in amplitudes seen mainly in the APB.
- higher peak amplitudes initially, followed by a phase of adaptation
- there are multiple "secondary peaks" during further writing which leads to further difficulty and prolongation of writing task
- the amplitudes after stopping writing and relaxation do not show prompt return to baseline as will be discussed below

This delayed time to relaxation – delayed "off set" was seen in the WC group (90%), the mean time taken being 33 seconds. The muscles which showed this trend included APB, ADP and trapezius. The mean amplitudes of these muscles between the two groups during the relaxation phase was much higher and statistically significant for EDC and trapezius (nearing significance for APB). Functional MR studies have shown persistent elevation in basal ganglia activity even after stopping finger tapping (Blood et al) [23], which corroborates with our findings.

The time of onset of muscle activation/ firing relative to APB was determined to identify the pattern of individual muscle recruitment. Majority of the healthy individuals showed a distal to proximal ontogeny. The sternomastoid, biceps and triceps were the muscles to show least activity. In contrast, the WC group showed earlier recruitment of the trapezius, EDC and arm muscles also showed a similar pattern. This early recruitment could be as a result of rapid ipsilateral overflow as a result of altered SMO (maladaptation). The other explanation could be use of the proximal muscles as an "adaptation" to overcome the dystonia which usually involved the forearm and hand muscles. The correlation between EMG activity in the contralateral limb can help to differentiate among the two phenomenologies.

Contralateral overt normal hand involvement and bihemispheric disturbances (using TMS, fMR) are well described in literature. [53, 54] The concepts of mirror dystonia and contralateral overflow have been defined, Sitburana et al identified high frequency of mirror movements, observations made from videos reporting 67% incidence. We expect

the incidence to be much higher using reliable EMG assessment. Using surface EMG from the same eight muscles in the contralateral limb, the following observations were made:

1. contralateral limb activity seen in all the WC subjects
2. higher rectified SEMG amplitudes especially from the trapezius and EDC
3. ontogeny showing proximal to distal pattern in the majority. (60%)

The implications of these observations need to be discussed. There could be increased bilateral central motor drive during voluntary activation of the dystonic limb leading to synchronized discharges from both the motor cortex. This combined with loss of cortico-cortical inhibition and increased corticospinal excitability could lead to the phenomenon. The exact reason for the ontogeny (proximal-distal) is not clear, contralateral overflow seems the most likely answer. As dystonic symptoms have been reported to occur in the normal limb subsequently, these findings could be consistent with probable "predystonia" of the clinically normal limb. Only longitudinal follow-up studies can confirm whether this phenomenon is progressive/ would even manifest as dystonia later.

The finding of contralateral activity can help to differentiate between "adaptation/ maladaptation" and "dystonia" especially with regard to proximal limb activity. It can also be useful to identify culprit muscles for chemodenervation and adaptive training/ EMG biofeedback.

Though it is well known that writing on a slant board improves the handwriting in WC, we could not objectively quantify any major differences by comparing the mean duration,

legibility of handwriting or rectified SEMG during writing normally and writing on a slant board which was done in 6 subjects. There was a trend towards more proximal and lesser distal muscle recruitment; however these findings will have to be validated with a larger sample size.

Two parameters: age more than 40 years and FMS 3 correlated with functional disability on Chi square tests, however only FMS showed significant statistical correlation on logistic regression analysis. More definitive associations can be traced using larger sample size.

Spectral analysis showed higher percentage shift in Mean Frequency of EMG towards lower frequency in the FHD group. This shift however was not statistically significant on comparison between the two groups. This could most plausibly reflect “reflex slowing” of recruitment secondary to metabolite (lactate) accumulation. These changes combined with the rectified EMG may also reflect: greater total muscle fiber recruitment, increased firing rate and synchronization of motor units.

Two major limitations were relatively small sample size and lack of fine wire electrodes. Many of the parameters will need further validation with larger sample size considering the heterogenous spectrum of involvement. Fine wire needle recordings into ADP could have given higher yields considering the fact that the location of the muscle was deep. Nevertheless, the study has given useful insights into the clinical manifestations using non-invasive surface EMG.

CONCLUSION

Surface EMG can provide a rational approach to clinical assessment and guide selection and monitoring of appropriate therapy in subjects with Focal Hand Dystonia. The clinical correlation of the various electrophysiological phenomenon can have important treatment implications and evolve novel therapies. Major observations included:

1. Heterogenous spectrum of activation and muscle recruitment suggesting individual variability.
2. "Earlier onset" (60%), higher SEMG amplitudes and "delayed offset" (90%) times in the FHD group. Time taken for writing was also significantly longer.
3. Proximal muscle activation earlier in FHD suggestive of rapid overflow, contralateral overflow also was present.
4. FMS correlated with functional disability.

SCOPE FOR FUTURE WORK

Considering the immense scope for research potential and the "felt need" for a proper treatment strategy, we would like to take this study further

1. do fMRI/PET studies in tandem with Electrophysiology studies (combine EMG correlates- look at the FCR reflex)
2. utilize TMS studies- to characterize the altered SMO and delineate the basis for ontogeny further- the importance being to see if one could devise treatment strategies- like EMG guided denervation, rTMS, Bio-feedback, peripheral FES (Functional Electrical stimulation) or a multi-disciplinary treatment approach design to ameliorate this functional disability.

BIBLIOGRAPHY

1. Ramazzini M. *Diseases of scribes and notaries*, 1713

2. Russottoa DT, Perlmutter JS. Task- specific dystonias. *Ann N Y Acad Sci*. 2008 October ; 1142: 179–199.

3. Sheehy MP, Marsden CD. Writer's cramp—a focal dystonia. *Brain* 1982;105:461–480.

4. Karp, B. Limb dystonia. In: Stacy, M., editor. *Handbook of Dystonia*. Informa Healthcare USA; New York, NY: 2007, Page 158.

5. Sheehy MP, Rothwell JC, Marsden CD. Writer's cramp. *Adv Neurol* 1988;50:457–472.

6. Weiss EM, Hershey T, Karimi M, et al. Relative risk of spread of symptoms among the focal onset primary dystonias. *Mov Disord* 2006;21:1175–1181.

7. Marion MH, Afors K, Sheehy MP. Problems of treating writer's cramp with botulinum toxin injections: results from 10 years of experience. *Rev Neurol* (Paris) 2003;159:923–927.

8. Singer C, Papapetropoulos S, Vela L. Use of mirror dystonia as guidance for injection of botulinum toxin in writing dysfunction. *J Neurol Neurosurg Psychiatry* 2005;76:1608–1609.

9. Cohen LG, Hallett M. Hand cramps—clinical features and electromyographic patterns in a focal dystonia. *Neurology* 1988;38:1005–1012.

10. Hughes M, McLellan DL. Increased coactivation of the upper limb muscles in writer's cramp. *J Neurol Neurosurg Psychiatry* 1985;48:782–787.

11. Cornella CL, Leurgans S, Wuu Joanne, et al. Rating scales for dystonia : a multicentre assessment. *Mov Disord* 2003 ;18 :303-312.

12. Waddy HM, Fletcher NA, Harding AE, Marsden CD. A genetic study of idiopathic focal dystonias. *Ann Neurol* 1991;29:320–324.

13. Gasser T, Windgassen K, Bereznai B, et al. Phenotypic expression of the DYT1 mutation: a family with writer's cramp of juvenile onset. *Ann Neurol* 1998;44:126–128.

14. Leube B, Hendgen T, Kessler KR, et al. Sporadic focal dystonia in Northwest Germany: molecular basis on chromosome 18p. *Ann Neurol* 1997;42:111–114.

15. Bhidayasiri R, Jen JC, Baloh RW. Three brothers with a very-late-onset writer's cramp. *Mov Disord* 2005;20:1375–1377.

16. Roze E, Soumare A , Pironneau I, et al. Case-control study of writer's cramp. *Brain* 2009: 132; 756–764.

17. Garraux G, Bauer A, Hanakawa T, et al. Changes in brain anatomy in focal hand dystonia. *Ann Neurol* 2004;55:736–739.

18. Delmaire C, Vidailhet M, Elbaz A, et al. Structural abnormalities in the cerebellum and sensorimotor circuit in writer's cramp. *Neurology* 2007;69:376–380.

19. Hanakawa T, Immisch I, Toma K, et al. Functional properties of brain areas associated with motor execution and imagery. *J Neurophysiol* 2003;89:989–1002.

20. Ibanez V, Sadato N, Karp B, et al. Deficient activation of the motor cortical network in patients with writer's cramp. *Neurology* 1999;53:96–105.

21. Odergren T, Stone-Elander S, Ingvar M. Cerebral and cerebellar activation in correlation to the action-induced dystonia in writer's cramp. *Mov Disord* 1998;13:497–508.

22. Preibisch C, Berg D, Hofmann E, et al. Cerebral activation patterns in patients with writer's cramp: a functional magnetic resonance imaging study. *J Neurol* 2001;248:10–17.

23. Blood AJ, Flaherty AW, Choi JK, et al. Basal ganglia activity remains elevated after movement in focal hand dystonia. *Ann Neurol* 2004;55:744–748.

24. Tempel LW, Perlmutter JS. Abnormal cortical responses in patients with writer's cramp. *Neurology* 1993;43:2252–2257.

25. Mink JW. The basal ganglia: focused selection and inhibition of competing motor programs. *Prog Neurobiol* 1996;50:381–425.

26. Perlmutter JS, Stambuk MK, Markham J, et al. Decreased [18F]spiperone binding in putamen in idiopathic focal dystonia. *J Neurosci* 1997;17:843–850.

27. Levy LM, Hallett M. Impaired brain GABA in focal dystonia. *Ann Neurol* 2002;51:93–101.

28. Hallett M. Pathophysiology of writer's cramp. *Hum Mov Sci* 2006;25:454–463.

29. Ibanez V, Sadato N, Karp B, et al. Deficient activation of the motor cortical network in patients with writer's cramp. *Neurology* 1999;53:96–105.

30. Hamano T., Kaji R., Katayama M, et al. Abnormal contingent negative variation in writer's cramp. *Clinical Neurophysiology* 1999;110: 508–515.

31. Hallet. Dystonia: abnormal movements result from loss of inhibition. *Adv Neurol* 2004;94:1–9

32. Panizza M, Lelli S, Nilsson J, Hallett, M. H-reflex recovery curve and reciprocal inhibition of H-reflex in different kinds of dystonia. *Neurology* 1990; 40: 824–828

33. Chen RS, Tsai CH, lu CS. Reciprocal inhibition in writer's cramp. *Mov Disord* 1995;10:556–561.

34. Chen R, Wassermann EM, Canos M, Hallett M. Impaired inhibition in writer's cramp during voluntary muscle activation. *Neurology* 1997;49:1054–1059.

35. Ridding MC, Sheean G, Rothwell JC, et al. Changes in the balance between motor cortical excitation and inhibition in focal, task specific dystonia. *J Neurol Neurosurg Psychiatry* 1995;59:493–498.

36. Rona S, Berardelli A, Vacca L, et al. Alterations of motor cortical inhibition in patients with dystonia. *Mov Disord* 1998;13:118–124.

37. Sohn YH, Hallett M. Disturbed surround inhibition in focal hand dystonia. *Annals of Neurology*;56:595–599

38. Rosenkranz K, Williamon A, Butler K, et al. Pathophysiological differences between musician's dystonia and writer's cramp. *Brain* 2005;128:918–931.

39. Lin PT, Ejaz A, Hallett M. Focal hand dystonia. *Practical Neurology* 2006;6:278-287

40. Bara-Jimenez W, Catalan MJ, Hallett M, Gerloff C. Abnormal somatosensory homunculus in dystonia of the hand. *Ann Neurol* 1998;44:828–831.

41. Quartarone A, Bagnato S, Rizzo V, et al. Abnormal associative plasticity of the human motor cortex in writer's cramp. *Brain* 2003;126:2586–2596.

42. Quartarone A, Rizzo V, Bagnato S, et al. Homeostatic-like plasticity of the primary motor hand area is impaired in focal hand dystonia. *Brain* 2005;128:1943–1950.

43. Quartarone A, Siebner HR, Rothwell JC. Task-specific hand dystonia: can too much plasticity be bad for you? *Trends Neurosci* 2006;29:192–199.

44. Byl N, Wilson F, Merzenich M, et al. Sensory dysfunction associated with repetitive strain injuries of tendinitis and focal hand dystonia: a comparative study. *J Orthop Sports Phys Ther* 1996;23:234–244.

45. Sanger TD, Tarsy D, Pascual-Leone A. Abnormalities of spatial and temporal sensory discrimination in writer's cramp. *Mov Disord* 2001;16:94–99.

46. Bara-Jimenez W, Shelton P, Hallett M. Spatial discrimination is abnormal in focal hand dystonia. *Neurology* 2000;55:1869–1873.

47. Putzki N, Stude P, Konczak J, et al. Kinesthesia impaired in FHD. *Mov Disord* 2006;21:754-760.

48. Meunier S, Garnero L, Ducorps A, et al. Human brain mapping in dystonia reveals both endophenotypic traits and adaptive reorganization. *Ann Neurol* 2001;50:521–527.

49. Kaji R, Rothwell JC, Katayama M, et al. Tonic vibration reflex and muscle afferent block in writer's cramp. *Ann Neurol* 1995;38:155–162.

50. Nowak DA, Rosenkranz K, Topka H, et al. Disturbances of grip force behaviour in focal hand dystonia: evidence for a generalised impairment of sensory-motor integration? *J Neurol Neurosurg Psychiatry* 2005;76:953–959.

51. Murase N, Kaji R, Shimazu H, et al. Abnormal premovement gating of somatosensory input in writer's cramp. *Brain* 2000;123:1813–1829.

52. Quartarone A, Bagnato S, Rizzo V, et al. Corticospinal excitability during motor imagery of a simple tonic finger movement in patients with writer's cramp**.** *Mov Disord* 2005 ;20(11):1488-95

53. Sitburana O, Wu LJ, Sheffield JK, et al. Motor overflow and mirror dystonia. *Parkinsonism Relat Disord* 2009;15(10):758-761.

54. Merello M, Carpintiero S, Cammarota A, et al. Bilateral mirror writing movements (mirror dystonia) in a patient with writer's cramp: functional correlates. *Mov Disord* 2006 ;21(5):683-9

55. Farmer SF, Sheean GL, Mayston MJ, et al. Abnormal motor unit synchronization of antagonist muscles underlies pathological cocontraction in upper limb dystonia. *Brain* 1998;121(Pt 5):801–814.

56. Balash Y, Giladi N. Efficacy of pharmacological treatment of dystonia: evidence-based review including meta-analysis of the effect of botulinum toxin and other cure options. *Eur J Neurol* 2004;11:361–370.

57. Jankovic J. Treatment of dystonia. *Lancet Neurol* 2006;5:864–872.

58. Djebbari R, du Montcel ST, Sangla S, et al. Factors predicting improvement in motor disability in writer's cramp treated with botulinum toxin. *J Neurol Neurosurg Psychiatry* 2004;75:1688–1691.

59. Tsui JK, Bhatt M, Calne S, Calne DB. Botulinum toxin in the treatment of writer's cramp: a double- blind study. *Neurology* 1993;43:183–185.

60. Simpson DM, Blitzer A, Brashear A, et al. Assessment: botulinum neurotoxin for the treatment of movement disorders (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 2008;70:1699– 1706.

61. Kruisdijk JJ, Koelman JH, Ongerboer de Visser BW, et al. Botulinum toxin for writer's cramp: a randomised, placebo-controlled trial and 1-year follow-up. *J Neurol Neurosurg Psychiatry* 2007;78:264–270.

62. Karp BI, Cole RA, Cohen LG, et al. Long-term botulinum toxin treatment of focal hand dystonia. *Neurology* 1994;44:70–76.

63. Priori A, Berardelli A, Mercuri B, Manfredi M. Physiological effects produced by botulinum toxin treatment of upper-limb dystonia—changes in reciprocal inhibition between forearm muscles. *Brain* 1995;118:801–807.

64. Gilio F, Curra A, Lorenzano C, et al. Effects of botulinum toxin type A on intracortical inhibition in patients with dystonia. *Ann Neurol* 2000;48:20–26.

65. Ceballos-Baumann AO, Sheehan G, Passingham RE, et al. Botulinum toxin does not reverse the cortical dysfunction associated with writer's cramp: a PET study. *Brain* 1997;120:571–582.

66. Taira T, Hori T. Stereotactic ventrooralis thalamotomy for task-specific focal hand dystonia (writer's cramp). *Stereotact Funct Neurosurg* 2003;80:88–91.

67. Cho CB, Park HK, Lee KJ, Rha HK. Thalamic deep brain stimulation for writer's cramp. *J Korean Neurosurg Soc* 2009;46:52-55.

68. Priori A, Pesenti A, Cappellari A, et al. Limb immobilization for the treatment of focal occupational dystonia. *Neurology* 2001;57:405–409.

69. Zeuner KE, Bara-Jimenez W, Noguchi PS, et al. Sensory training for patients with focal hand dystonia. *Ann Neurol* 2002;51:593–598 .

70. Zeuner KE, Hallett M. Sensory training as treatment for focal hand dystonia: A 1-year follow-up. *Mov Disord* 2003;18:1044–1047**.**

71**.** Espay AJ, Hung SW, Sanger TD, et al. A writing device improves writing in primary writing tremor. *Neurology* 2005;64:1648-1650.

72. Berwick DM, Winickoff DE. The truth about doctors' handwriting: a prospective study. *BMJ* 1996;313:1657–8

ANNEXURE

PROFORMA FOR DATA COLLECTION (FHD STUDY)

Name Age Sex

Occupation

Educational status

Duration of symptoms

Symptoms

Treatment status

Fahn Marsden score

Any comorbidities

Writing task:

Timing: Rest

Think/ imagine

Write

Relax

Stop recording

Comments on recording